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The American Heart Journal

VOL. VI AUGUST, 1931 No. 6

Original Communications

OCCURRENCE AND SIGNIFICANCE OF ELECTROCARDIOGRAMS DISPLAYING LARGE Q-WAVES IN LEAD III*

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IN A RECENT publication, Pardee[2] called attention to electrocardiograms exhibiting large Q-waves in Lead III, and found that 63 per cent of the forty-three patients in his group had the anginal syndrome. The possibilities of this observation prompted me to carry out an investigation in a larger series of cases.

MATERIAL

The electrocardiograms in the files at The Mayo Clinic were carefully searched, and in approximately 70,000 records, 300 tracings were found which conformed to the criteria demanded by Pardee. The incidence of the electrocardiograms with large Q-waves in Lead III cannot be accurately established, owing to the fact that many tracings that previously had been considered to be essentially normal had been destroyed. It is possible that among these were some with large Q-waves in Lead III.

Pardee made his selection on the following grounds: (1) Electrocardiograms of left axis deviation, or normal axis deviation, were chosen; those of right axis deviation were excluded, for in these Q_3 is normal; (2) the excursion of the Q-wave in Lead III was more than 25 per cent of the greatest excursion of the QRS complex in any lead; (3) records with notching deformity of the QRS complex in Lead III, the so-called W and M complexes, were excluded; and (4) in all records chosen there was, in Lead III, an initial downward deflection (Q), succeeded by a definite upward deflection (R) and no S-wave.

These criteria were rigidly adhered to in the selection of my cases. Pardee investigated the incidence of these electrocardiograms as they may be found in examination of persons whose hearts are apparently normal, and found only two such records in 277 such cases, an inci-

*From the Section on Cardiology, The Mayo Clinic.

dence of only 0.7 per cent. In discussing the occasional occurrence of a large Q-wave in Lead III in electrocardiograms of apparently normal hearts, he suggested the possibility of unusual distribution of the branches of the auriculoventricular bundle, and that a high diaphragm may contribute to the appearance of this abnormally large Q-wave. In The Mayo Clinic series of 300 cases in which there were large Q-waves in Lead III only three patients (1 per cent) with apparently normal hearts were found. Wolferth,[3] in studying the electrocardiograms of 700 normal subjects, did not find any instance of a large Q-wave in Lead III. Later in this paper the material studied by Pardee, and that studied by Wolferth will be employed as a composite, control group of 977 normal persons.

CLINICAL CORRELATION

The correlation of the electrocardiograms under consideration with the clinical diagnoses in my series differed somewhat from that of Pardee. The greatest incidence of the characteristic electrocardiographic changes occurred in cases of hypertensive heart disease; that is, of the 300 characteristic electrocardiograms, 120 (40 per cent) were obtained in cases of this type (Table I). The anginal syndrome without hypertension occurred in 76 cases or 25.3 per cent of those which gave the characteristic electrocardiogram, and hypertensive heart disease, associated with the anginal syndrome, in 39 cases (13 per cent). Arteriosclerotic heart disease, without the anginal syndrome and without hypertension, occurred in 33 cases (11 per cent).

TABLE I

CORRELATION OF LARGE Q-WAVES IN LEAD III WITH CLINICAL CONDITIONS IN 300 CASES

CLINICAL DIAGNOSIS	CASES	PER CENT
Hypertensive heart disease	120	40.0
Anginal syndrome	76	25.3
Hypertensive heart disease with anginal syndrome	39	13.0
Arteriosclerotic heart disease without anginal syndrome	33	11.0
Total	268	89.3
Exophthalmic goiter	8	2.8
Syphilitic aortitis with aortic insufficiency	7	2.3
Rheumatic heart disease:		
mitral stenosis	5	1.7
aortic stenosis	3	1.0
Chronic pericarditis with adhesions	1	0.3
Congenital heart defect; probably patent ductus arteriosus	1	0.3
Enlarged heart of undetermined origin	1	0.3
Arteriosclerotic disease of vessels of leg	1	0.3
Exertion dyspnea without clear evidence of cardiac disease	2	0.7
Apparently normal heart	3	1.0
Total	32	10.7

In the three groups, in which there was clinical evidence of coronary disease, there were 148 cases (49.3 per cent of 300). For comparison,

Pardee's data are presented in Table II where it is seen that the anginal syndrome occurred in 27 cases (63 per cent). Pardee speculated on the possibility of narrowing of the coronary arteries having taken place in 8 other cases (18 per cent); thus, he considered the theoretical possibility that coronary disease was present in 81 per cent of his cases.

TABLE II

CLINICAL CORRELATION OF LARGE Q-WAVES IN LEAD III WITH CLINICAL CONDITIONS IN FORTY-THREE CASES (PARDEE)

CLINICAL DIAGNOSIS	CASES	PER CENT
Anginal syndrome	27	62.8
Syphilitic aortic insufficiency	1	2.3
Myocardial fibrosis:		
with congestion	4	9.4
with arrhythmia	1	2.3
Rheumatic heart disease:		
active, with mitral insufficiency	1	2.3
aortic insufficiency, with or without mitral disease	2	4.7
mitral insufficiency	0	0.0
mitral stenosis, with or without mitral insufficiency	1	2.3
Arteriosclerosis with hypertension	1	2.3
Hypertension with arrhythmia	1	2.3
Hyperthyroid (enlarged) heart; enlargement determined by percussion and roentgenograms; patient aged 54 years	1	2.3
Pregnancy; a record after delivery did not show a large Q_3 (normal heart)	1	2.3
Effort syndrome, including the group of cases showing neurocirculatory asthenia (normal heart)	2	4.7
Normal heart	0	0.0
Congenital heart defect	0	0.0
Arteritis obliterans	0	0.0

It is possible of course that in some of the cases that I have classified as examples of hypertensive heart disease there may have been associated coronary disease, for relatively high coexistence of these conditions is seen at necropsy. However, critical review of these records did not justify a classification other than that given. It may be noted that the four groups embodying hypertensive and arteriosclerotic heart disease, combined, include 268 cases (89.3 per cent of the entire 300).

In analyzing the remaining thirty-two cases (10.7 per cent) of the series, a rather varied aggregation of conditions is found (Table I). Considering the predominant influence of these conditions on the ventricles it becomes evident that the majority of disorders exerted strain on the left ventricle (20 cases, 6.6 per cent of 300). It is even possible that the remaining 9 pathological conditions (mitral stenosis, congenital cardiac defect, enlarged heart of undetermined origin, and dyspnea on exertion without clear-cut evidence of cardiac disease; Table I) were complicated by lesions that likewise produced strain predominantly on the left ventricle.

TABLE III

CLINICAL DATA			DATA OBTAINED AT NECROPSY	
AGE AND SEX	DIAGNOSIS	ELECTROCARDIOGRAM	WEIGHT OF HEART, GM.	PATHOLOGICAL FEATURES
56 M	Anginal syndrome	Sinus arrhythmia; negative T-wave Lead I, depressed R-T segment Leads I and II; elevated R-T segment Lead III	395	Advanced, generalized arteriosclerosis with sclerosis of the coronary arteries and myocardial fibrosis
54 M	Coronary thrombosis with cardiac infarction; essential hypertension	Sinus rhythm; negative T-waves in Leads I and II; R-T segment depressed in Leads I and II and elevated in Lead III	420	Coronary sclerosis with thrombotic occlusion; infarction of left ventricle and mural thrombosis
53 M	Hypertensive heart disease with anginal syndrome	Sinus rhythm; negative T-wave Lead I; R-T segment depressed in Lead I and elevated in Lead III	662	Marked coronary sclerosis and cardiac hypertrophy; mural thrombosis of right ventricle
58 M	Hypertensive heart disease	Sinus rhythm; negative T-wave in Lead III	550	Cardiac hypertrophy
60 F	Hypertensive heart disease	Sinus rhythm; negative T-wave in Lead III	385	Cardiac hypertrophy
62 M	Hypertensive heart disease	Sinus rhythm; negative T-wave Lead III; R-T segment depressed in Leads I and II; elevated in Lead III	400	Cardiac hypertrophy
67 M	Arteriosclerotic heart disease	Sinus rhythm	290	A few small epicardial hemorrhages; moderate calcification at the base of the right and left coronary cusps of the aortic valve; slight sclerosis of the coronary arteries and moderate sclerosis of the aorta; patent foramen ovale
36 F	Syphilitic aortitis with aortic insufficiency	Sinus rhythm; negative T-wave in Leads I and II	400	Marked syphilis of the aorta with enormous dilatation of the left ventricle
52 M	Chronic endocarditis with aortic insufficiency; anginal syndrome	Sinus rhythm; diphasic T-waves in Leads I and II; negative T-wave in Lead III		Chronic aortic endocarditis with insufficiency; cardiac hypertrophy and dilatation; aortitis (syphilitic?) with fusiform aneurysm of ascending aorta; coronary sclerosis

Data Obtained at Necropsy.—Only 9 cases were available in which pathological study of the hearts was carried out. The detailed data are shown in Table III. This group is obviously too small to permit definite conclusions, although certain facts are clearly portrayed. In 8 cases, the hearts were definitely hypertrophied, ranging in weight from 385 to 700 gm. Three cases of hypertensive heart disease occurred without associated involvement of the coronary arteries. This lends support to the conception that the dominant condition is hypertensive heart disease, as is brought out in Table I. Four cases presented the anginal syndrome, and five cases presented well-marked evidence of coronary disease. In all the cases there was evidence of disease of the left ventricle.

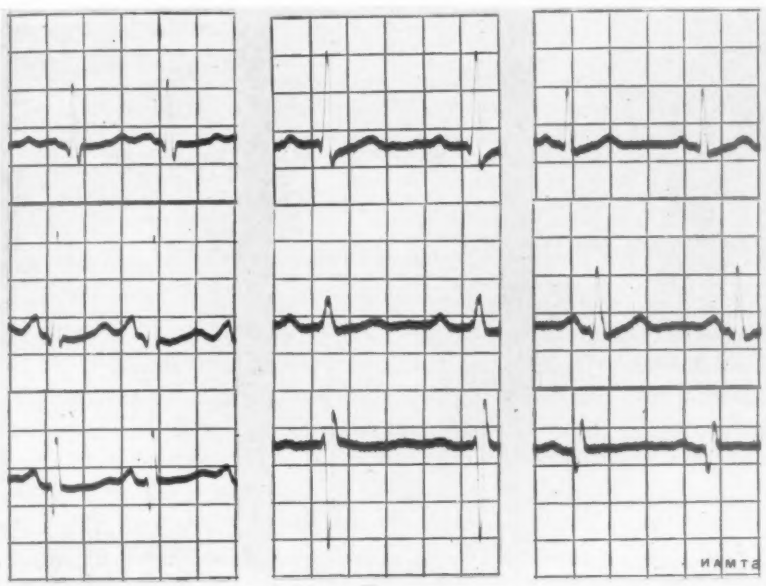

Fig. 1.—Electrocardiograms which contain large Q-waves in Lead III.

DATA ON CONTROL SERIES

The composite group[2, 3] of electrocardiograms, made from 977 normal persons, revealed only two cases (0.2 per cent) in which there were large Q-waves in Lead III. This extremely low incidence is of considerable significance. In order to obtain further control data as to the incidence of these electrocardiograms in cases of cardiac disease I took records, in each of which the cardiac condition corresponded, as nearly as possible, to one of the four conditions which were seen most frequently in my series of 300 cases. This selection was made without knowledge of the nature of the electrocardiograms. Of 120 cases of hypertensive heart disease thus chosen, in twelve (10

per cent) there were large Q-waves in Lead III. Large Q-waves in Lead III occurred in five cases (7 per cent) of seventy-six cases in which the anginal syndrome was present, in four cases (10 per cent) of thirty-four cases of hypertensive heart disease with the anginal syndrome, and in one case (3 per cent) of thirty-three cases of arteriosclerotic heart disease without the anginal syndrome and without hypertension.

ASSOCIATED ELECTROCARDIOGRAPHIC FEATURES IN THE SERIES OF 300 CASES

In the majority of records (214 cases, 71.4 per cent of 300) the direction of the T-waves was normal. That is, they were upward in all leads in eighty-eight cases (29.4 per cent of 300) and upright in Leads I and II and downward in Lead III in 126 cases (42 per cent of 300). This incidence is slightly greater than that found by Pardee (63 per cent).

TABLE IV

ASSOCIATED SIGNIFICANT T-WAVE NEGATIVITY

T-WAVE NEGATIVITY	PARDEE SERIES		WILLIUS SERIES	
	NUMBER	PER CENT	NUMBER	PER CENT
Lead I	1	2.5	28	9.3
Leads I and II	4	9.0	20	6.6
Leads II and III	11	25.0	27	9.0
Leads I, II and III	0	0.0	11	3.7
Total	16	37.2	86	28.6

The incidence of significant T-wave negativity is shown in Table IV, and is there compared with the observations of Pardee. The occurrence of T-wave negativity according to leads in my series varies considerably from that of Pardee, particularly as far as Leads II and III are concerned. He stated that the greater frequency of inversion of T-2 and T-3 (25 per cent) as compared with T-1, with or without T-2 (11.5 per cent) is noteworthy. In my series, however, this ratio is reversed; T-wave negativity in Leads II and III occurred in only 9 per cent of the cases, whereas 19.6 per cent of the cases displayed T-wave negativity in Lead I, Leads I and II and in all leads. These ratios are in accord with the conception that there was strain predominantly on the left ventricle, as already mentioned, and conform to the views of Barnes and Whitten[1] regarding T-wave negativity independent of cardiac infarction.

The only other significant electrocardiographic features encountered in my series were in eighteen cases (6 per cent of 300) of auricular fibrillation. Two of these cases were associated with T-wave negativity in Leads II and III.

Thus, in the complete group of 300 cases, the only significant electrocardiographic feature in 198 cases (66 per cent) was the large Q-wave in Lead III. Therefore, this abnormality may be looked on as being an additional diagnostic sign that may be of reliable significance

when the electrocardiogram is otherwise unaltered. It appears to occur predominantly in diseases exerting their influence chiefly on the left ventricle, but insufficient reports of necropsy are available at this time to permit definite conclusions to be formed. Although the anginal syndrome occurred frequently (38.3 per cent) when this form of electrocardiogram was present, it was by no means limited to cases of which the anginal syndrome was a feature.

SUMMARY

Three hundred cases in which there were electrocardiograms with large Q-waves in Lead III, according to the criteria of Pardee, are presented. The majority of these records (268 or 89.3 per cent) were obtained in examination of patients who had one of the following conditions: hypertensive heart disease, the anginal syndrome, hypertensive heart disease accompanied by the anginal syndrome, or arteriosclerotic heart disease not accompanied by the anginal syndrome or hypertension. The remaining thirty-two patients (10.7 per cent) had miscellaneous conditions, but the majority of them had diseases that exert their influence chiefly on the left ventricle. Only three cases (1 per cent) in which the patients apparently had normal hearts were found. In 198 cases (66 per cent of 300) the large Q-wave in Lead III was the only significant electrocardiographic feature present, permitting the conclusion that this abnormality may be considered as an additional diagnostic sign. In the composite group of 977 normal persons studied by various observers there were only two cases (0.2 per cent) in which large Q-waves occurred in Lead III.

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THYROTOXIC CIRCULATORY SYMPTOMS WITH LOW METABOLIC RATE*

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HYPERTHYROIDISM is one of the well recognized causes of heart disease. In the earlier stages, sinus tachycardia is the commonest disturbance of the circulation. Auricular flutter is encountered at times, as electrocardiographic records have demonstrated. In the later stages of hyperthyroidism, auricular fibrillation and congestive heart failure are frequently seen. If the damage to the myocardium has not been too great, the fibrillation may cease following subtotal thyroidectomy.

In frank hyperthyroidism with increase in the metabolic rate, the recognition of the nature of the circulatory disturbance is not difficult. In the case of "masked" hyperthyroidism, however, painstaking study of the case is required to bring out the underlying thyroid factor, as Levine,[1] Hamburger and Lev[2] and others have shown. Levine considers transient auricular fibrillation the most characteristic manifestation. The heart sounds are peculiarly loud and hyperactive. Failure to obtain the usual reduction in rate through digitalization is suggestive. Increase in the metabolic rate, combined with such data as the general appearance of the patient; greater comfort in cold weather than in warm; brief attacks of diarrhea and vomiting; alert, quick movements; often a peculiar stare to the eyes and a tremor of the fingers; transient glycosuria—all of these, with increased basal metabolic rate, in the absence of exophthalmos or obvious goiter, lead to the diagnosis. Coexisting organic heart disease renders the diagnosis even more difficult. Levine found complete relief or marked improvement following subtotal thyroidectomy. Hamburger and Lev discuss hyperthyroidism masked by congestive heart failure, by anginal heart failure, associated with organic heart disease of rheumatic or arteriosclerotic type, or masquerading as diabetes mellitus or as pernicious hyperemesis.

Cases in every way similar but with a low metabolic rate may be encountered, as we have reported elsewhere.[3] With increasing experience, we are finding the condition much more frequently, and believe that early recognition with operation is of great importance.

The evidence of circulatory disturbance may not be striking in some instances, as the first of the following cases illustrates.

*From the Department of Internal Medicine, University of Cincinnati.

CASE 1.—R. E. M., male, aged 34 years, was admitted to the hospital November 17, 1930, for the treatment of duodenal ulcer which had caused a rather severe hematemesis. He was placed on the Sippy treatment and improved satisfactorily, but complained of a nervous tension and of palpitation. It was noted that there was a slight stare and lid-lag but no exophthalmos. There was no visible goiter, but palpation revealed a moderately enlarged adenomatous gland, over which a faint continuous murmur was audible. There was an instability of the pulse, the rate being between 90 and 100. There was a strong pulsation in the abdominal aorta. The blood pressure was increased, averaging between 160/80 and 170/90 mm. The heart action was forceful. Relative dullness measured 2×9 cm. The sounds were loud and clear, the rhythm was regular. There was a weak systolic shock at the apex. There was slight fine tremor in the fingers. The skin was of normal texture and moist. The remainder of the physical examination was negative. On November 17, the basal metabolic rate was −17 per cent; on November 24 the rate was −32 per cent; on November 29 a third determination also gave a rate of −32 per cent. Differential count showed 27 per cent lymphocytes. Subtotal thyroidectomy was performed December 3. A fairly large adenomatous gland was found. For two days after operation thyrotoxic symptoms increased but were controlled by luminal and by increasing the dose of Lugol's solution, which had been started prior to operation. Thereafter the patient made an uneventful recovery. Nine days after operation the basal metabolic rate was −12 per cent. A month after operation the metabolic rate was −10 per cent, the pulse rate was normal and the blood pressure 120/80 mm. The nervousness and palpitation disappeared and the patient was feeling perfectly well.

This case represents a mild form of thyrotoxic circulatory disturbance. Palpitation, consciousness of the heart's action and tachycardia were the only symptoms referable to the circulation. There was nervousness and a tendency to perspire. Physical findings indicating thyrotoxicosis were the lid-lag and stare, goiter, tremor of the fingers, overactive heart with loud sounds, moderate tachycardia, and increase in the pulse pressure. The basal metabolic rates would seem to exclude a hyperthyroidism, yet the symptoms and physical signs which suggested a mild thyrotoxicosis cleared up after subtotal thyroidectomy just as in cases of hyperthyroidism. Three weeks of absolute bed rest prior to operation had been of no avail. The findings in no way suggested hypothyroidism. The metabolic rate rose to the lower limit of normal following operation.

CASE 2.—Mrs. P. M., married, aged 70 years, was seen in June, 1930, complaining of palpitation, "smothering spells" at night, consciousness of the heart's action and nervousness. These symptoms had been present with varying degree for several years. There was increased perspiration. The weight had not varied more than a few pounds. On physical examination the patient was found to be short and stout. There was no exophthalmos, but a suggestive stare was noted; there was no lid-lag. The neck was short and the thyroid was palpated with some difficulty; it was firm and nodular, a typical adenomatous goiter. The heart was enlarged to the left, the apex being in the fifth interspace, 12 cm. from the midline, and slightly heaving. The blood pressure was 200/120 mm.; the pulse rate 96. There was a fine tremor of the fingers. A determination of the basal metabolic rate could not be made at this time. The patient was given Lugol's solution, ten drops, three times a day for two weeks. There was improvement in all the symp-

toms, and the blood pressure decreased to 150/90 mm.; pulse rate 84. In September the patient entered the hospital for operation. The symptoms and physical findings remained as they were at the original examination. The basal metabolic rate was −6 and +4 per cent. The blood pressure was 196/110 mm. A subtotal thyroidectomy was performed, from which the patient made a good recovery. She has been feeling well since then and has been entirely relieved of her symptoms. Her blood pressure following operation was 152/84 mm.

CASE 3.—Mrs. K. H., aged fifty-one years, was seen November 20, 1928. She was emotional, crying easily. She complained of tachycardia, consciousness of the heart's action, a feeling of nervous tension and tremor of the hands. These symptoms had been troublesome for about one year. There was no increase of perspiration and no loss of weight. The patient has had a goiter for many years. Physical examination showed a woman 5 ft. 2½ in. tall, weight 146 lb. The color was good. There was no exophthalmos, lid-lag or stare. The thyroid was enlarged and firm, the left lobe somewhat larger than the right. The consistence was uneven, indicating the presence of adenomata. The heart was normal in size, the sounds loud and clear, the rate 100, rhythm regular. The blood pressure was 136/76 mm. There was a fine tremor of the fingers. The remainder of the physical examination was negative. Differential count showed 58 per cent lymphocytes. Red and white counts and hemoglobin were normal. On November 27 the basal metabolic rate was +1 and +7. Subtotal thyroidectomy was done January 2, 1929. An adenomatous goiter was found. Recovery was uneventful. On March 2, 1929, the patient was re-examined. She felt better in all respects. The nervousness had disappeared. There was no longer throbbing in the arteries, and the hands were steady. The pulse rate was 84, blood pressure 126/74 mm. Basal metabolic rates were +5 and +8 per cent.

CASE 4.—Mrs. C. E. M., aged fifty-nine years, was seen September 9, 1929. For eight years she had had attacks of diarrhea which lasted about one week. She had about six attacks a year. For more than a year she had lost strength and had lost 18 pounds in weight in the last six months. She had been very nervous for several months, and her hands had been unsteady in sewing and writing. There was no history of rheumatic fever. The patient was a small woman, height 5 feet, weight 112 pounds. She looked older than her age. There was no exophthalmos, but a definite stare and lid-lag were noted. There was a marked tremor of the fingers. Both lobes of the thyroid were enlarged and adenomatous. The heart apex was 8.5 cm. to the left in the fifth interspace. Relative dullness measured 2 × 10 cm. Auricular fibrillation was present. The heart rate was 32 to the quarter minute. There was a systolic apical murmur. The pulmonic second sound was not accentuated. The blood pressure was 150/80 mm. for the largest beats. There was no edema. Basal metabolic rates on September 10 were +4 and +7. Subtotal thyroidectomy was performed on September 17, from which the patient made a good recovery. One week following operation, the heart became regular. Subsequently, the tremor and nervousness disappeared and the patient gained 20 pounds. The basal metabolic rate was not determined following operation. Symptomatic recovery has been complete.

COMMENT

These cases illustrate the importance of a careful investigation of the thyroid and, when indicated, the beneficial results which may be obtained through operation. *The basal metabolic rate*, while very helpful when it is elevated, *is a sign which should be ignored, when normal or*

subnormal, in the presence of unmistakable evidence of thyrotoxic symptoms and signs.

The circulatory manifestations are often more pronounced than in the cases cited. Every case of auricular fibrillation should have careful study of the thyroid; rheumatic heart disease may be associated with thyroid disease. Operation may largely relieve the circulatory symptoms. At times the goiter is substernal, being demonstrable only by x-ray examination.

The explanation of the low basal metabolic rate in the cases under discussion is not clear. The symptoms and signs are those of hyperthyroidism rather than of myxedema. Yet subtotal thyroidectomy either raises the metabolic rate when it is subnormal or, when normal, leaves it practically unchanged. Signs of myxedema with low metabolic rate would undoubtedly follow if too much of the gland were removed, but as yet we have not encountered such instances among our cases. It is noteworthy, too, that both subjective and objective improvement may be obtained with Lugol's solution prior to operation, just as in hyperthyroidism.

An important fact to keep in mind in connection with the thyroid heart is that it is the one type of heart disease which is preventable.

In any patient in whom the pulse pressure and the blood pressure are increased without apparent cause, thyroid disease should be suspected. Usually the systolic pressure is elevated; often both systolic and diastolic pressures are raised.

In all patients with cardiac neuroses, the possibility of disease of the thyroid gland should never be lost sight of. Careful study of the case often reveals a "burned out" hyperthyroidism or an adenomatous thyroid. Subtotal thyroidectomy may result in cure.

In patients with organic heart disease, the thyroid may be a contributing, at times a dominant, factor in the production of symptoms. The frequency with which a thyroid dyscrasia is found, depends upon the care exercised in looking for it.

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THE STATUS OF THE HEART IN MYXEDEMA*

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THE condition of the cardiovascular system in myxedema is still controversial. Zondek in 1918,[1] Assmann in 1919,[2] Meissner in 1920,[3] and Fahr in 1925[4] and in 1927,[5] have described cases in which dilatation of the heart both to the right and to the left and signs of cardiac failure were relieved only by thyroid therapy. Willius and Haines,[6] studying a large number of cases of myxedema in 1925, found no characteristic cardiovascular changes.

As to the electrocardiographic changes in myxedema, Zondek described cases in which the P- and T-waves were absent, and reappeared after thyroid medication. Fahr found the P-wave present in his cases; he considered a negative T-wave in Leads I and II the most characteristic change. Lueg[7] and Nobel, Rosenblüth and Samet[8] state that the increased resistance of the skin may account for the "absence" of P- and T-waves. This explanation is, according to Wilson,[9] untenable, since the electrical capacity introduced into the circuit by the high resistance of the myxedematous skin should be eliminated by proper preparation of the skin before the electrocardiogram is taken.

Thatcher and White[10] in 1926 published a careful study of the electrocardiograms in 14 cases of myxedema in all of which there was a low T-wave in Lead II. They also noted a general decrease in the amplitude of all electrocardiographic deflections in all leads before treatment, with an increase after treatment with thyroid extract. They concluded that there is a distinct parallelism between the height of the T-wave in the electrocardiogram and the basal metabolic rate in hypothyroidism.

Willius and Haines,[6] in analyzing the electrocardiograms in 55 cases of myxedema, found the curves, aside from graphic evidence suggestive of ventricular preponderance, to be normal in 28 of them and abnormal in 12. The abnormalities in the latter group consisted chiefly in T-wave negativity, with disappearance of negativity after thyroid medication.

Reid and Kenway[11] recently studied the electrocardiograms of 260 patients with various clinical conditions, who had a basal rate between minus 10 per cent and minus 48 per cent, and discovered no electrocardiographic findings characteristic of low basal metabolism. The definitely myxedematous subjects, of which there were 5, all showed low T-waves; 4 showed low P-waves as well.

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With the object of obtaining additional evidence bearing upon the condition of the heart in myxedema, I have gone through the records of all patients diagnosed as having myxedema during the last eight years at the University of Michigan Hospital. Cases diagnosed "hypothyroidism" were not included in this study, since this diagnosis was usually based on a slightly lowered basal rate, often not lower than minus 20 per cent, and since no roentgenologic or electrocardiographic examinations were made in these cases. There were 18 cases, diagnosed as myxedema, in which electrocardiograms were available. In all of these patients the basal metabolic rate was minus 25 per cent or lower, with the exception of one who had received a few doses of desiccated thyroid before the first determination. In this case the basal rate was minus 18 per cent. There were only 7 cases in which electrocardiograms were made both before and after treatment.

Of the 18 subjects studied, 13 were women and 5 men. The average age was forty-seven years; 4 patients were under thirty-nine years, 5 between forty and forty-nine years, and 9 over fifty years of age. All of them presented the typical signs and symptoms of myxedema. In practically all of the cases the heart sounds were described as faint; in some instances they were almost inaudible. Seven patients presented symptoms and signs of first degree cardiac insufficiency; in 5 of these the heart was enlarged; in the other two it appeared to be normal in size. These patients complained of dyspnea on exertion and showed pitting edema over the ankles and feet.* Eleven patients had no cardiac failure. Fluoroscopic and teleroentgenographic examinations of the heart were carried out in 15 cases. In the reports of the fluoroscopic examination the heart is often described as showing indistinct or feeble pulsation of its borders. The heart was enlarged, either on roentgen ray or on physical examination, in 9 patients; 5 of these showed an aortic or hypertensive type of enlargement with a prominent aortic knob. In all of these cases either hypertension or general arteriosclerosis was present. It was considered not enlarged in 9 cases, 3 of which showed a rather prominent aortic knob in the remainder the heart was apparently normal in shape. Seven of the entire group showed peripheral and retinal arteriosclerosis; 8 had no evident arteriosclerosis; in 3 patients, the condition of the peripheral and retinal vessels was not mentioned. Of the group of 7 who showed general arteriosclerosis, 2 were between forty-five and forty-nine years, and 5 over fifty years of age. The presence of arteriosclerosis

*Erythrocyte counts and hemoglobin determinations were made in 17 cases. The average red cell count was 3.8 million per c. mm., and the average hemoglobin value (Sahli) was 73 per cent. Of the seven patients who showed pitting edema of the lower extremities, all had hemoglobin readings above 68 per cent and red blood cell counts above 3.8 million, per c. mm., except one with 3.5 million. It is not probable that the pitting edema of the lower extremities observed in these patients was due to the anemia. Four patients in which the red counts and hemoglobin readings were below 3.5 million and 68 per cent respectively, did not show pitting edema.

may have been related more to the process of senility than to the duration of myxedema, since of the 6 cases with myxedema of ten or more years' duration, only 2 showed moderate peripheral arteriosclerosis, and 4 showed none. Seven patients showed a systolic blood pressure exceeding 150 mm. Hg., or a diastolic pressure in excess of 90 mm. Hg. or both. In the others there was no evidence of hypertension. Only one of the 6 patients who had suffered from myxedema for ten years or more had hypertension. Apparently, the blood pressure is often low in patients with myxedema of long duration. Excluding the one case in which the first basal rate was made after several doses of thyroid extract had been given, the average basal metabolic rate of the 17 subjects was minus 33 per cent.

ELECTROCARDIOGRAPHIC FINDINGS

The average heart rate, determined from the initial electrocardiograms made before treatment was begun, was 71 per minute, while the average rate taken during the first basal metabolic rate determinations was 9 beats less, or 62 per mitnute. The P-R interval was essentially normal, except that it was slightly prolonged in 3 subjects; in two of these it measured 0.2 second and in one 0.22 second. The duration of the initial ventricular deflection, QRS, varied between 0.06 and 0.08 second, and was, therefore, normal in all cases. The minimum, average, and maximum amplitudes in millimeters of the deflections P, R, S, and T are given in Table I. Compared with simi-

TABLE I

AMPLITUDE IN MILLIMETERS OF DEFLECTIONS IN EIGHTEEN CASES OF MYXEDEMA

	LEADS	P	R	S	T
Minimum		0.	1.2	0.4	−2.0
Mean	I	0.4	5.5	0.5	−0.1
Maximum		1.0	10.0	2.0	1.6
Minimum		0.	0.	0.	−1.5
Mean	II	0.6	5.1	0.5	−0.3
Maximum		1.4	11.0	4.0	1.0
Minimum		−1.0	0.	0.	−1.2
Mean	II	0.2	1.6	2.0	−0.2
Maximum		0.5	6.0	10.0	1.0

Note: Each millimeter = 10^{-4} volt. One patient showed auricular fibrillation.

larly tabulated values obtained in 52 normal students by Lewis,[12] the mean values of the P-deflections in Leads II and III are only one-half and one-fourth, respectively, of the mean figures for the same leads of Lewis' normals. The mean amplitudes of the R-waves in Leads II and III are likewise only one-half and one-fourth the normal values. The difference in the amplitudes of these deflections is too great to be entirely accounted for by the difference in the average age between this group and that of normal students studied by Lewis.

Still more definite and conspicuous are the changes in the T-deflections. The minimum, average, and maximum values of the T-waves in the myxedema cases are far below the normals of Lewis. The average amplitude of the T-deflection in Lewis' normal subjects was: Lead I, 1.93 mm.; Lead II, 2.46 mm.; and Lead III, 0.61 mm.; while the corresponding averages in myxedema are: minus 0.1, minus 0.3, and minus 0.2 mm. respectively. In fact, the maximum height of this deflection in Leads I and II of my series is definitely less than the

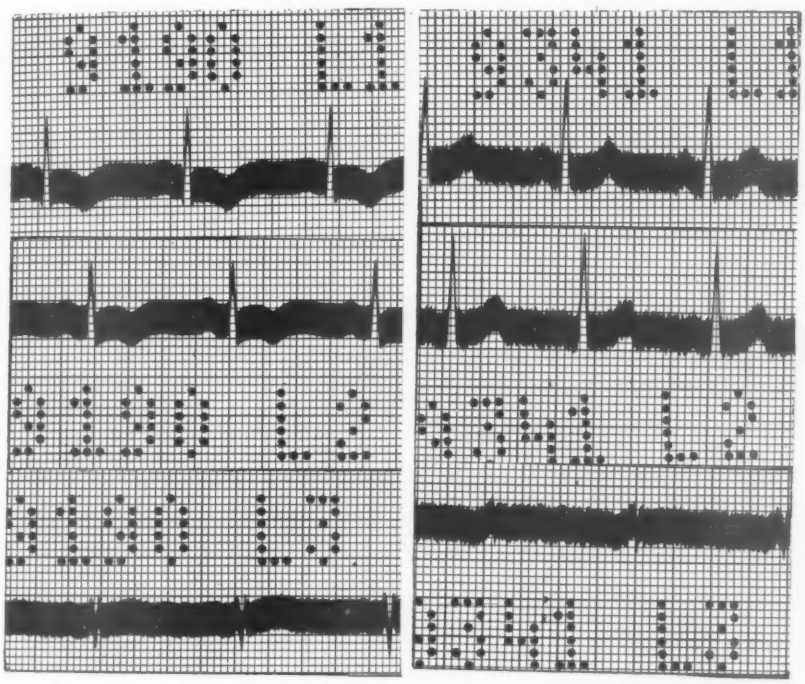

Fig. 1.—(Case 3.) E.k.g. No. 9190, taken September 29, 1927, before thyroid therapy, when basal metabolic rate was minus 36 per cent. E.k.g. No. 9341, taken October 22, 1927, after thyroid therapy when basal metabolic rate was plus 8 per cent.

average height in the corresponding leads of Lewis' series. Table II gives the direction of the T- and P-deflections of the 18 cases before treatment. Inversion of T in Lead I, or in Leads I and II occurred in 6 patients; inversion of T in Leads II and III occurred in 6 cases; inversion of T in all leads occurred once; and flat T-waves in all three

TABLE II

DIRECTION OF T- AND P-WAVES IN EIGHTEEN CASES OF MYXEDEMA

	T-WAVES			P-WAVES			
LEAD	INVERTED	FLAT	UPRIGHT	INVERTED	FLAT	UPRIGHT	DIPHASIC
I	6	5	7	0	1	16	0
II	10	5	3	0	1	16	0
III	8	6	4	3	8	5	1

leads occurred twice. The T-deflections were, therefore, definitely abnormal in 15 out of 18 patients. When upright, they were not more than 1.6 mm. in height in Lead I, and not more than 1.0 mm. in the other two leads.

In only 7 patients of this series was an electrocardiogram taken after the basal rate was brought back to an approximately normal level by thyroid medication. As changes in the electrocardiograms following treatment constitute definite evidence that the deviations from normal found in the curves before treatment are attributable to myxedema, the data in each of these 7 subjects are tabulated in detail in Table III. It will be noticed that although the P- and QRS-deflections tended to

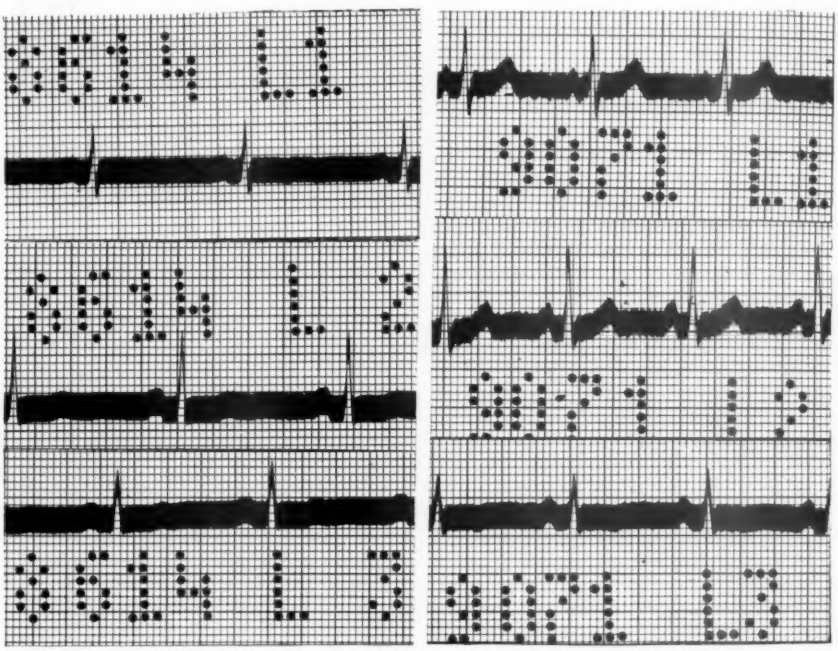

Fig. 2.—(Case 2.) E.k.g. No. 8614, taken June 21, 1927, before thyroid therapy, when basal metabolic rate was minus 27 per cent. E.k.g. No. 9071, taken September 8, 1927, after thyroid therapy, when basal metabolic rate was plus 2 per cent.

rise following treatment, the chief alteration consisted in the direction and amplitude of the T-deflections in Leads I and II, where all inverted or flat T-deflections became definitely upright, and low T-waves assumed a greater amplitude. There is, however, a tendency in all but one case for the T-wave in the third lead to become or remain flattened or inverted following treatment. Figs. 1, 2, and 3 illustrate the changes in the electrocardiograms of three of these patients produced by treatment.

In only one patient (Case 4) were teleroentgenograms taken both before and after thyroid treatment. This patient presented slight

cardiac insufficiency, with a transverse cardiac diameter of 15 cm. before taking desiccated thyroid. When the basal rate was brought up to minus 9 per cent, the transverse cardiac diameter was 12.75 cm. In the other cases, no follow-up x-ray examination of the heart was made.

It would not be profitable here to speculate upon the significance of the inversion of the final ventricular deflection. Whether it is due to myocardial anoxemia, consequent upon diminished blood flow through the coronary vessels, to a myxedematous change in the heart muscle,

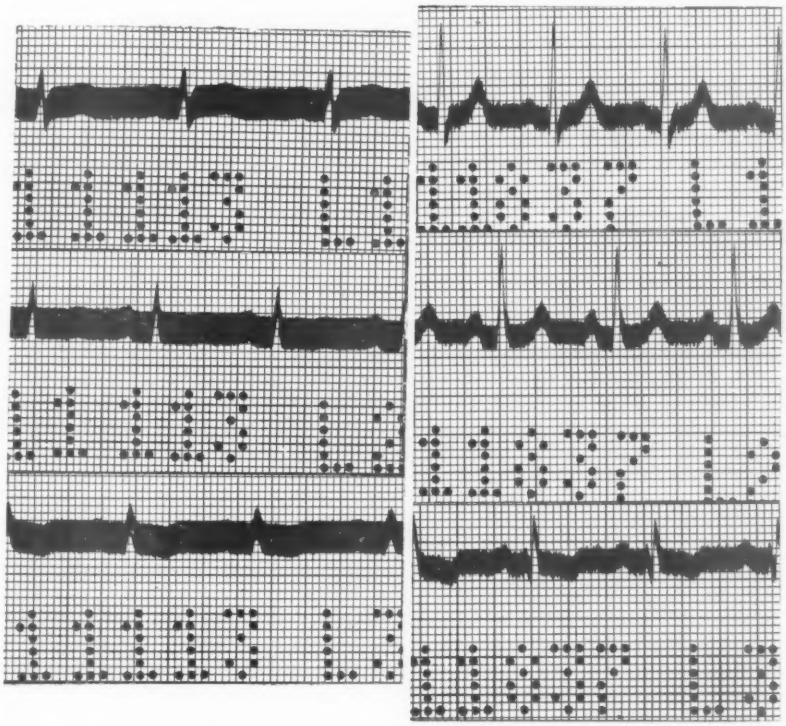

Fig. 3.—(Case 4.) E.k.g. No. 11113, taken November 23, 1928, before thyroid therapy, when basal metabolic rate was minus 31 per cent. E.k.g. No. 11837, taken May 9, 1929, after thyroid therapy when basal metabolic rate was minus 9 per cent.

or to some other cause, is at present uncertain. Whatever the actual mechanism underlying the T-wave inversion, it is probably dependent upon a functional change in the gradient of the ventricular musculature, involving a change in the duration of systole in the various parts of the ventricles. It is interesting to note again that all inverted or flat T-deflections became definitely upright after the basal metabolic rate was brought back to an approximately normal level, indicating that the cardiac damage is not necessarily permanent.

In the seven cases, which presented signs of cardiac insufficiency before treatment, all such signs disappeared after thyroid therapy.

TABLE III

ELECTROCARDIOGRAPHIC DATA OF SEVEN MYXEDEMA PATIENTS BEFORE AND AFTER THYROID TREATMENT

NO.	SEX	AGE	DATE	ELECTROCARDIOGRAM AMPLITUDE IN MILLIMETERS EACH MM. = 10^{-4} VOLT						BMR %	HEART AND PERIPHERAL BLOOD VESSELS
				LEAD	P	T	QRS	P-R (SEC.)	RATE		
1.	M	58	Jan. 3, 1927 (Before treatment)	I	+0.4	−0.2	+8.0		56	−28	Heart enlarged, and hypertensive in type. Aortic arch prominent. Slight general arteriosclerosis.
				II	+0.2	−0.2	+5.0	0.18			
				III	−0.2	flat	−3.0				
			April 25, 1927 (After treatment)	I	+0.4	+2.0	+8.0		54	− 9	
				II	+0.6	+1.0	+7.0	0.18			
				III	flat	−1.2	−2.8				
2.	F	44	June 21, 1927 (Before treatment)	I	+0.2	flat	+5.0 / −2.0		60	−27	Heart normal in size and shape. Aortic arch not prominent. No general arteriosclerosis.
				II	+0.8	flat	+8.0	0.17			
				III	+0.5	+0.4	+3.5				
			Sept. 8, 1927 (After treatment)	I	+0.6	+2.0	+5.0		80	+ 2	
				II	+1.6	+1.8	+8.0	0.15			
				III	+1.0	−0.2	+3.5				
3.	F	51	Sept. 29, 1927 (Before treatment)	I	+0.2	−2.0	+7.0		70	−36	Heart slightly enlarged and of hypertensive type. Aortic arch normal. No mention of peripheral arteries.
				II	+0.5	−1.5	+6.0	0.16			
				III	flat	+0.6	−2.0				
			Oct. 22, 1927 (After treatment)	I	+1.0	+1.8	+10.0		80	+ 8	
				II	+0.4	+1.8	+9.0	0.15			
				III	−0.8	flat	−1.0				

TABLE III—CONT'D

NO.	SEX	AGE	DATE	ELECTROCARDIOGRAM AMPLITUDE IN MILLIMETERS EACH MM. = 10^{-4} VOLT						BMR %	HEART AND PERIPHERAL BLOOD VESSELS
				LEAD	P	T	QRS	P-R (SEC.)	RATE		
4.	F	51	Nov. 23, 1928 (Before treatment)	I	+0.2	+0.4	+3.5 / −2.0		75	−31	Heart markedly enlarged, especially the left ventricle. Aortic arch slightly prominent. Transverse diameter, 15 cm. No general arteriosclerosis.
				II	+0.6	−0.2	+4.0	0.18			
				III	+0.2	−0.8	+2.5				
			May 9, 1929 (After treatment)	I	+0.8	+3.2	+11.0 / −2.0		96	− 9	Definite diminution in size of cardiac shadow in teleroentgenogram. Present transverse diameter, 12.75 cm. Aortic arch still prominent.
				II	+1.4	+2.0	+11.0	0.16			
				III	+1.2	−1.0	+4.0				
5.	F	24	Dec. 19, 1930 (Before treatment)	I	+1.0	+0.6	+10.0		72	−34	Heart not enlarged. No x-ray examination. No peripheral arteriosclerosis.
				II	+1.4	+0.8	+11.0	0.15			
				III	+0.4	flat	+1.2				
			Mar. 26, 1931 (After treatment)	I	+1.0	+2.2	+8.0		68	−11	
				II	+1.4	+3.0	+12.5	0.15			
				III	+0.4	+1.0	+4.5				
6.	F	65	Jan. 29, 1931 (Before treatment)	I	+0.6	+0.4	+4.0 / −0.4		75	−28	Heart normal in size and shape.
				II	+0.8	flat	+1.4	0.20			Aorta not mentioned.
				III	flat	−0.6	−2.5				Marked peripheral arteriosclerosis.
			Mar. 20, 1931 (After treatment)	I	+1.0	+1.8	+7.0		100	− 4	
				II	+1.8	+1.2	+2.0	0.18			
				III	+0.6	−1.0	−5.0				
7.	M	49	Mar. 6, 1931 (Before treatment)	I	+1.0	−0.4	+5.0		90	−47	Heart slightly enlarged, more toward left, than right.
				II	+1.0	−1.0	+6.0	0.20			Aortic arch slightly widened.
				III	flat	−0.4	+1.8				
			Apr. 23, 1931 (After treatment)	I	+1.0	+0.6	+9.0		95	−16	No peripheral arteriosclerosis.
				II	+1.2	+0.6	+9.0	0.18			
				III	+0.8	flat	+1.0 / −1.0				

The definite response of these patients to substitution therapy and their failure to respond to digitalis are evidence that the clinical syndrome which has been referred to as a "myxedema heart" does exist in a certain proportion of patients with high grade myxedema and is due to a lack of sufficient thyroid secretion. Although cardiac insufficiency occurred in only a little more than one-third of these patients, the electrocardiogram demonstrated cardiac abnormalities in more than three-fourths of them. Perhaps, only a small number develop definite signs of cardiac weakness because of the diminished metabolism and activity which characterize the disease.

SUMMARY

This study is based upon an analysis of the hospital records of eighteen cases of definite myxedema with an average basal metabolic rate on admission of minus 33 per cent. The average age of these patients was forty-seven years. Seven of these patients showed evidence of cardiac insufficiency; nine had enlargement of the heart; seven had hypertension; and in seven a definite generalized arteriosclerosis was noted. There did not appear to be any definite relation between the presence of hypertension or arteriosclerosis and the duration of the myxedematous state. The symptoms and signs of cardiac weakness disappeared under thyroid medication. In all cases, the electrocardiogram showed P-waves and QRS-waves of relatively small amplitude. The most striking abnormality was the flattening or inversion of the T-deflection which disappeared after treatment in the seven cases in which the electrocardiographic examination was repeated after the basal metabolic rate had returned to normal.

The writer wishes to acknowledge his indebtedness to Dr. Frank N. Wilson for his encouragement and valuable suggestions.

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THE MECHANISM OF DEATH OF THE HUMAN HEART AS RECORDED IN THE ELECTROCARDIOGRAM*

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THE mode of death of the human heart, while it has claimed the attention of clinicians from time to time, has been mainly of academic interest. The demonstration in recent years that certain measures designed to revive a dying myocardium may at times be successfully employed makes desirable an analysis of existing knowledge of the sequence of events which immediately precedes the cessation of cardiac activity. Hearts which have apparently ceased to beat have resumed contraction following the intracardiac injection of adrenalin, after manual massage, or from the mechanical irritation caused by needle puncture alone as pointed out by Hyman.[1] The therapeutic use of oxygen has served to support a severely damaged heart muscle during periods of profound weakness until functional recovery has made possible resumption of a circulation adequate for the continuation of life.

It is the purpose of this paper to analyze the cases previously recorded, to supplement these with five additional reports, and to determine any possible therapeutic application of our existing knowledge of the dying human heart.

REVIEW OF THE LITERATURE

The first reference to electrocardiographic studies of the dying human heart is by Rohmer[2] who reported before the Section of Pediatrics of the Deutscher Naturforscher und Aerzte his observations in three fatal cases of diphtheria. He believed that the records showed complete dissociation of auricles and ventricles and noted further that the form of the QRS group was abnormal. So far as can be determined, these observations were never published as a paper.

In 1912 Robinson[3] made records of seven patients who died of acute infections (two of poliomyelitis, one of pneumococcus meningitis, four of pneumonia). Cardiac activity persisted for from six to thirty-five minutes after clinical death had occurred. In four cases, ventricular activity outlasted the auricular, while in two, the auricles continued to beat after the ventricles had stopped. Both auricles and ventricles ceased simultaneously in the remaining case. "Marked slowing of the rate of cardiac activity always occurred and there was usually distinct delay in the conduction time between auricles and ventricles. Com-

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plete dissociation was seen in three cases. Ventricular fibrillation occurred in two cases, in one of which the ventricles again established a regular rhythm. Evidence of auricular fibrillation was never seen. Characteristic changes in the ventricular electrical complex occurred in all these cases. They consisted of a decrease in the size of the R-wave and an increase in the size of the T-wave, and a tendency to a fusion of these waves. There was usually but little change in the duration of the ventricular complexes as the cardiac activity gradually ceased." From these observations, Robinson concluded that "when death occurs from an acute infectious disease, there is no one point in the human heart which may be considered as the 'ultimum moriens.'"

Electrocardiographic records were made by Halsey[4] during the death of a patient from bronchopneumonia. The heart rate slowed markedly, with a gradual prolongation of auriculoventricular conduction and a change in the form of QRS. An idioventricular rhythm appeared and auricular activity ceased. Ventricular fibrillation appeared shortly before the death of the heart.

The first records reported of patients dying of intrinsic cardiac disease were those of Dieuaide and Davidson.[5] In two cases electrocardiograms were taken during the death of the heart, while in a third case, the last record was taken three hours before death. The first two patients could probably be classified as cases of arteriosclerotic-hypertensive heart disease. The third case was one of rheumatic heart disease. Certain features were common to all three cases from an electrocardiographic standpoint, namely, a gradual slowing of cardiac rate, together with lengthening of P-R, QRS, and Q-T intervals; diminution of the amplitude of R and T; and A-V nodal rhythm or complete dissociation of auricles and ventricles. Various arrhythmias were observed, including auricular and ventricular extrasystoles, ventricular tachycardia, and auricular and ventricular fibrillation. Transient ventricular fibrillation occurred in the first case after all evidence of auricular activity had disappeared. Death occurred following a series of abnormal complexes, presumably of ventricular origin, which gradually slowed in rate and decreased in amplitude. In the second case, complete dissociation of auricles and ventricles also occurred. There was transient auricular fibrillation and there were brief runs of ventricular tachycardia. In the third case, transient ventricular tachycardia was observed three hours before death.

In an excellent study based on observations in twenty cases, Schellong[6] noted the frequency of A-V nodal rhythm, and found that this was often interrupted by beats of sinus origin. He believed that a lengthening of the P-R interval always went parallel with a decrease in rate during the first stage of death of the heart and that these changes were due to vagus activity. Complete auriculoventricular dissociation was found to occur in dying hearts, not as the result of a conduction

disturbance, but whenever the sino-auricular frequency fell below that of the A-V node. However, partial heart-block was not uncommon. Two cases showing auricular fibrillation died with gradual slowing of the circus movement. Schellong stated that the appearance of ventricular fibrillation depended upon the ability of the heart muscle to form ectopic impulses of sufficient frequency, regardless of the presence or absence of auricular fibrillation. In the two cases of ventricular fibrillation observed by him, both developed after a ventricular tachycardia. The T-waves in the dying hearts were noted to increase in size and to become positive even when previously negative.

Willius[7] reported four cases in detail and referred to two others in his series in which he found that, as death approached, auricular activity always ceased before that of the ventricles. Auricular fibrillation was present twice at the beginning of electrocardiographic study, but did not occur as an intercurrent event. Transient auricular flutter occurred once. A-V nodal rhythm was present in five cases. Complete heart-block was found three times, sino-auricular standstill twice, prolonged conduction and partial heart-block each once. Periods of cardiac standstill occurred in three cases, lasting 9.4 seconds in each of two patients, and 11.4 seconds in the third. Ventricular fibrillation occurred in four cases, and was terminal in three. A tendency to fusion of R and T was found in three cases. The four patients reported fully consisted of two cases of hyperthyroidism, one of rheumatic heart disease, and one of rheumatic heart disease with concurrent bacterial endocarditis.

In a study of ventricular tachycardia complicating digitalis therapy, Reid[8] recorded a change from ventricular tachycardia to a terminal ventricular fibrillation in one case.

Kahn and Goldstein[9] made observations on seven cases in all of which the sinus node failed first as shown by the establishment of A-V nodal rhythm. Intraventricular conduction defects were common. Ventricular fibrillation was present in two of their cases, once as a terminal event. In their summary, these authors stated that "the cessation of the normal auricular contraction stimulus seems to be the critical phenomenon in the process of death. Before this happens, the sinus node shows irritability and depression in various sequences and degrees and it is probable that if the disturbance could be controlled before cessation of sinus function, recovery might occur. After this happens, it is known experimentally that the heart will not recover although reoxygenated."

In seventeen cases reported by Martini and Sekell[10] the first change was a decrease in rate in most instances. Fatigue of the S-A node led to an A-V nodal rhythm. A new "X" wave frequently appeared between S and T. There was no constant form of the T-wave, but there was a tendency for the R and T waves to merge. In these cases the electrical manifestations did not persist long after clinical death, nine

minutes and thirty-eight seconds being the longest interval recorded. The authors concluded that no constant "ultimum moriens" could be found but that most often it was probably the A-V node.

Willius[11] recently summarized the data on this subject and stated "the fairly uniform onset of nodal rhythm, with marked slowing of the heart, and the varied phases of block that frequently are associated with these characteristics, are suggestive of marked vagal action. These phenomena are present at about the time that death appears to have occurred and when, undoubtedly, a marked degree of both cardiac and cerebral asphyxia is present. Cerebral or cardiac asphyxia, or both, have been produced experimentally and graphic transitions have appeared which are similar to those that have been produced by the dying human heart. The later changes observed, namely, long periods of com-

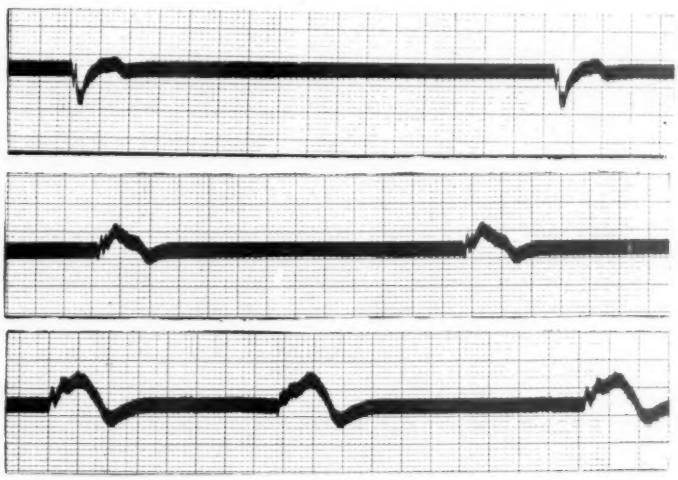

Fig. 1.—Case 1. Leads I, II, and III. About six minutes before clinical death. For full description of this and subsequent figures see text.

plete cardiac asystole, the fusion of component waves, and ventricular fibrillation may result from more profound changes which occur in the musculature itself." Also, in dying, "there is little difference between the records from patients with normal hearts and those from patients with advanced heart disease."

At a recent meeting of the Berliner Medizinische Gesellschaft, Professor v. Hoesslin[12] stated that he had observed electrical activity in hearts for a half-hour or more after clinical death. Ventricular fibrillation was rarely of long duration. Attempts to bring about a restoration of cardiac activity once standstill had occurred were more likely to succeed when the heart was not severely diseased.

CASE REPORTS

CASE 1.—M. S., a 55-year-old unmarried Irish woman, was admitted to the hospital because of gangrene of the left great toe. She was found to have general

arteriosclerosis and a somewhat enlarged heart with a tortuous aorta by x-ray examination. The past history was unimportant. The blood pressure was 112/72 mm. Amputation through the knee was performed, and on the fifth day after operation she complained of difficulty in breathing and pain over the precordium. She rapidly became dyspneic, cyanotic, and pulseless. The electrocardiograms were taken during clinical death, which was believed to have been due to pulmonary embolism. Necropsy was not performed.

Discussion of the Electrocardiograms.—The first electrocardiogram was taken about fifty minutes after the onset of symptoms and six minutes before clinical death (Fig. 1). The record shows bizarre complexes, presumably of ventricular origin, occurring somewhat irregularly

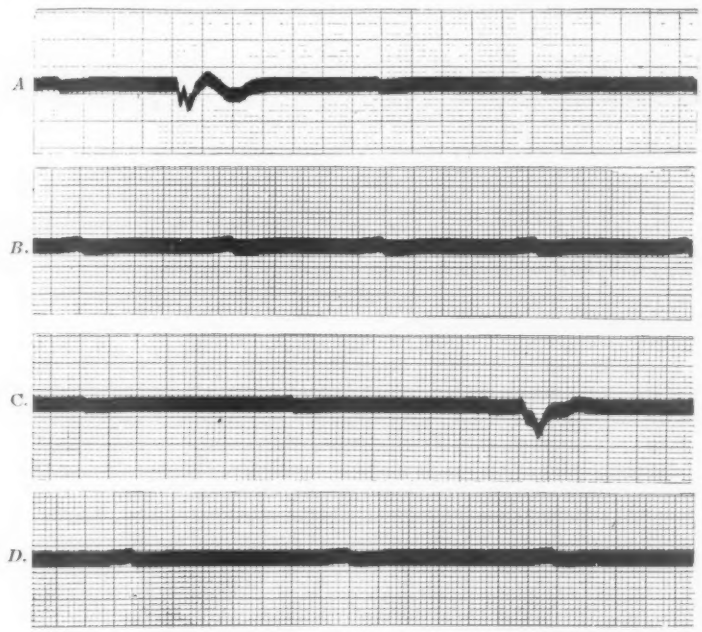

Fig. 2.—Case 1, *A* and *B*. Leads I and II. Taken during clinical death. *C* and *D*. Leads I and II. A few seconds after the preceding.

and at a rate of about 26 per minute. The rate is a little more rapid in Lead III than in Lead I of this record. The main deflection is downward in Lead I and upward in Lead III. In the third lead occur very slight deviations from the base line that may be due to auricular activity.

A second record was taken about two minutes after the first (Fig. 2 *A* and *B*), during the occurrence of clinical death. Throughout this record auricular contractions alone are present with the exception of a single bizarre ventricular complex in the early part. The P-waves, which are upright, occur regularly at a rate of 60 per minute.

The third record was practically continuous with the second. The auricles continue to beat for five minutes after clinical death. The rhythm has become increasingly regular and the rate shows gradual

slowing. Again in this record, a single bizarre ventricular complex occurs. This is the last evidence of ventricular activity. The auricles outlast the ventricles by about fifteen or twenty seconds (Fig. 2 *C* and *D*).

CASE 2.—C. T. was a 52-year-old Jewish salesman who was admitted to the hospital in uremia. He was found to have a blood pressure of 185/110 mm., general arteriosclerosis, and a large heart. There was no evidence of cardiac insufficiency. The blood showed a profound secondary anemia, evidence of marked nitrogen retention and acidosis. A loud precordial friction rub was heard. His course was progressively downhill. On the fourth day in the hospital he developed auricular fibrillation. There was a terminal bronchopneumonia. On the morning of the tenth day he had two convulsions and shortly thereafter died. Autopsy showed a chronic glomerulonephritis with general arteriosclerosis, cardiac hypertrophy, acute fibrinous pericarditis, and lobular pneumonia.

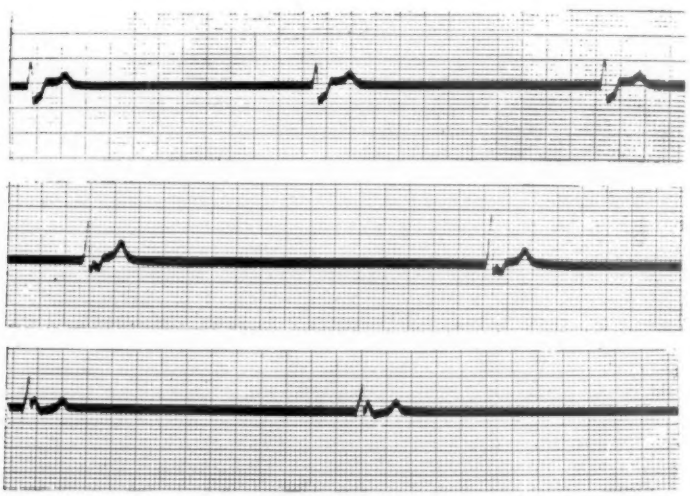

Fig. 3.—Case 2. Leads I, II, and III. About two minutes before clinical death.

Discussion of the Electrocardiograms.—The first electrocardiogram was taken on the fourth day, shortly before the auricles began to fibrillate. The record shows sinus rhythm with a rate of 94. The P-waves are all upright and there is some notching of P2. The P-R interval is 0.17. S3 is notched. The T-waves are upright, and those in Leads I and II are unusually prominent. There is an elevation of the S-T interval in all leads but this is not very marked.

The second electrocardiogram was taken six days later during the death of the patient. The record was started at 10:20 A.M. and was practically continuous until 10:24 A.M. when the last evidence of electrical activity was seen. Clinical death of the patient took place at 10:22 A.M., two minutes before the death of the heart. The record begins with a series of regular beats at a rate of 36. Apparently these beats originate in the lower portion of the A-V node with retrograde con-

duction to the auricles, as shown by inversion of P-waves following the QRS complexes (Fig. 3). This rhythm is occasionally interrupted by ectopic ventricular beats without compensatory pause. These beats sometimes replace the beats of nodal origin without disturbance of the rhythm (Fig. 4, *A* and *B*). At one place complete cardiac standstill occurs, lasting 7.2 seconds, followed by a ventricular contraction of the type seen previously, whereupon nodal rhythm is resumed for the space of four beats. Following this series, a succession of four ventricular complexes appears. There is again a period of cardiac standstill, lasting 13 seconds, interrupted once more by a contraction of

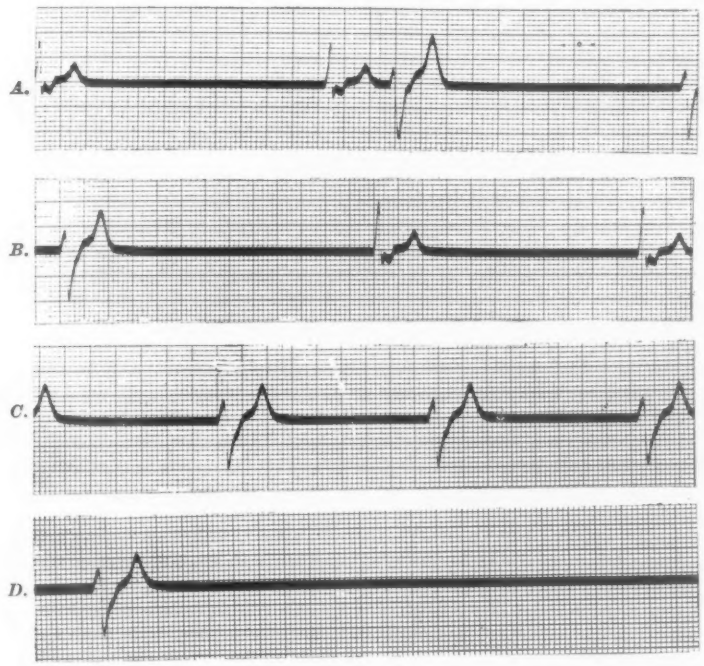

Fig. 4.—Case 2. Lead II. *A* and *B*, About two minutes before clinical death. *C*, Ventricular rhythm preceding cardiac death. *D*, Last evidence of cardiac activity.

ventricular origin. Three more nodal beats appear, of usual form, followed by a succession of ventricular complexes with an irregular rhythm marking the end of cardiac activity. There is no change in form in these terminal complexes, nor is there any diminution in their amplitude (Fig. 4, *C* and *D*).

CASE 3.—L. S. was a 55-year-old contractor who entered the hospital in a comatose state and was found to have syphilitic aortitis with a superimposed subacute bacterial endocarditis. His blood Wassermann reaction was four plus in both antigens and repeated blood cultures showed non-hemolytic streptococci constantly present. An electrocardiogram was taken on the third day in the hospital. On the twelfth day, after gradual improvement in the clinical condition, the patient had several attacks of unconsciousness during which his pulse rate was 34

and regular. Following one of these attacks he died. An electrocardiogram was taken a few minutes before, but not actually during, the clinical death of the patient. An autopsy was not permitted.

Discussion of the Electrocardiograms.—The first record was taken on the third day in the hospital and shows a sinus rhythm with prolonged A-V conduction. The P-R interval is 0.24 sec. The P-waves are upright in the first two leads and partly inverted in Lead III. The ventricular rate is 96. The QRS complexes are somewhat wider than normal measuring 0.13 sec., but this may be partly discounted by the fact that the patient had a very high skin resistance. R_1 and R_2 are notched. T_1 is inverted, while T_2 and T_3 are upright. There is a slight reciprocal displacement of the S-T interval in the first and third

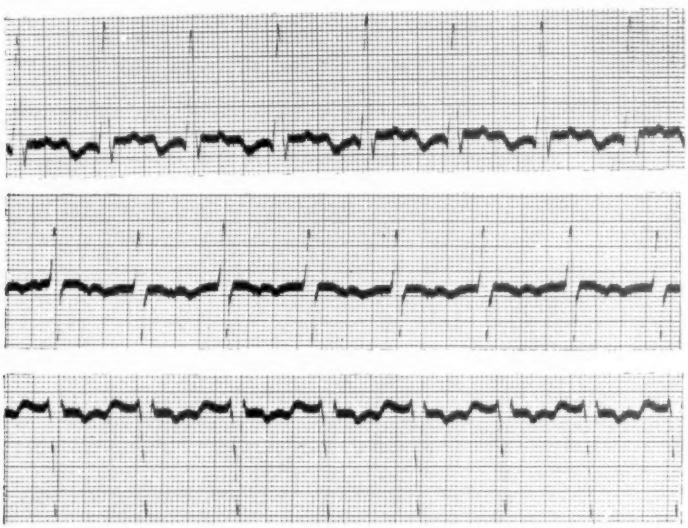

Fig. 5.—Case 3. Leads I, II, and III. Nine days before death.

leads. As the patient was not receiving digitalis, it was thought that the record was definitely indicative of myocardial damage (Fig. 5).

The second record, taken just before clinical death of the patient, begins with a series of P-waves, irregularly spaced, and without any ventricular response. These are succeeded by a short run of bizarre ventricular complexes, varying in form and amplitude with a slight irregularity of rhythm (Fig. 6 *A*). During this phase, no definite P-waves are to be found. Then P-waves reappear and are seen among the varying ventricular complexes, but complete dissociation between auricles and ventricles apparently exists (Fig. 6 *B*). At this point, all evidence of ventricular activity ceases, and for the space of about half a minute, nothing can be seen except irregularly spaced P-waves which have become inverted (Fig. 6 *C*). At the conclusion of the record, several bizarre ventricular complexes appear, all evidence of auricular

activity ceases, and the record ends with a regular series of ventricular complexes with deeply inverted T-waves, and a gradual change in the form of QRS (Fig. 6 *D*). The record ended approximately one to two minutes before the clinical death of the patient.

CASE 4.—D. J. was a 45-year-old housewife with mitral stenosis of long-standing, who entered the hospital for the second time because of cardiac insufficiency. During the two weeks before death, her course was one of progressive failure. She had a persistent slight fever but the heartbeat was slow and regular. An autopsy was not performed.

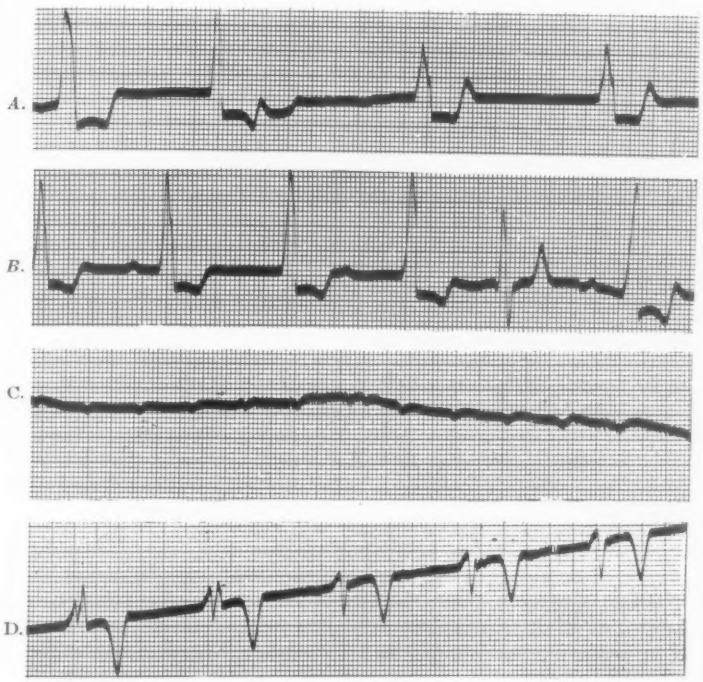

Fig. 6.—Case 3. About two minutes before clinical death. *A*, Lead I. *B*, Lead I. *C*, Lead II. *D*, Lead III.

Discussion of the Electrocardiograms.—The first electrocardiogram was taken four months before her death during her first admission to the hospital. It was characterized by marked "low voltage," a rapid rate, right ventricular preponderance, and showed in addition an inversion of the T-wave in Lead III. In subsequent records the rate was slower and the voltage within normal limits. This was the case in the record taken at the time of her second admission two weeks before death. The only additional finding at this time was that T_2 as well as T_3, had become inverted (Fig. 7).

The next electrocardiogram was started one to two minutes before clinical death. Marked irregularity of the sinus node is present. The P-waves are inconspicuous in the first lead but prominent and upright

in Leads II and III. The A-V conduction time is slightly prolonged. The intraventricular conduction time is 0.16 seconds and the ventricular complexes are bizarre in form, giving the picture commonly ascribed to block of the left bundle branch (Fig. 8).

Fig. 7.—Case 4. Leads I, II, and III. Two weeks before death.

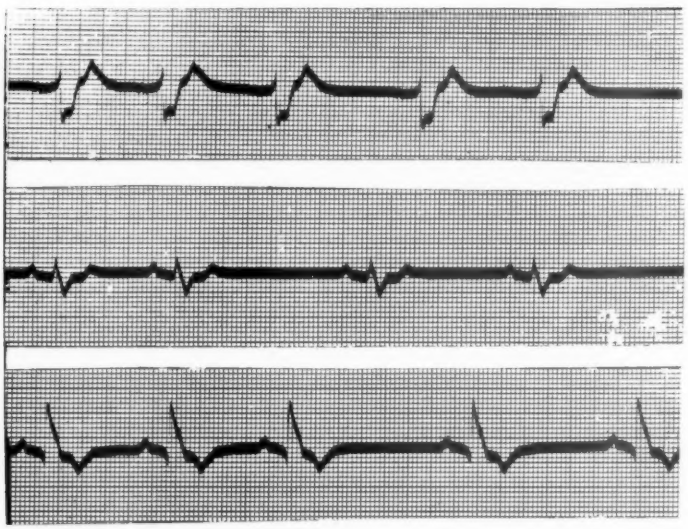

Fig. 8.—Case 4. Leads I, II, and III. About two minutes before clinical death.

The final record, taken during clinical death, shows a series of beats arranged in pairs resembling those in the previous Lead II. Occasional P-waves occur and are followed by ventricular complexes. These are seen in Fig. 9 *A*. In these sequences the P-R interval is 0.18 to 0.28 seconds.

The record was resumed after the lapse of a few seconds. All evidence of ventricular activity has disappeared. A few slight deflections from the base line are seen (Fig. 9 *B*). They probably represent auricular contractions. The rhythm is extremely irregular. Eventually all evidence of electrical activity ceases (Fig. 9 *C*).

CASE 5.—J. B. a 66-year-old white man had had increasing congestive heart failure for a year before admission. He was brought into the hospital in a moribund condition and died the day after admission.

Discussion of the Electrocardiograms.—The first record was taken about twenty-four hours before the death of the patient. It shows a sinus tachycardia with a rate of 120. Large numbers of auricular and

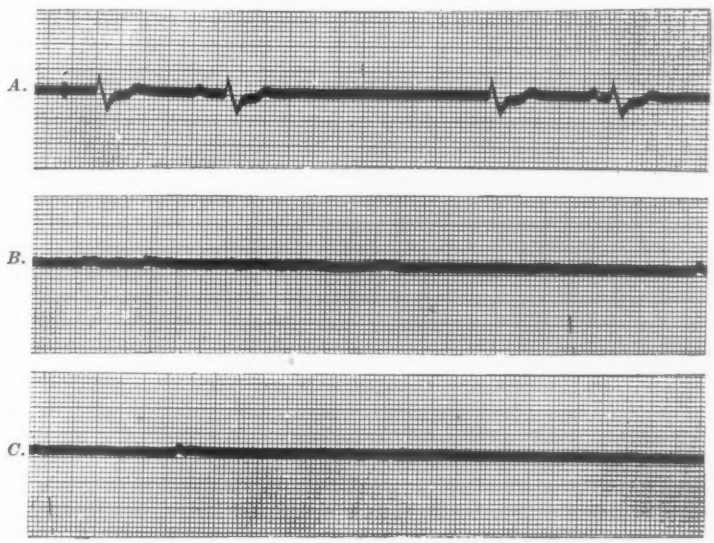

Fig. 9.—Case 4. *A*, Lead II. Approximately during clinical death. *B*, Lead II. A few seconds after the preceding. *C*, Lead II. End of cardiac activity.

nodal extrasystoles are present. The P-R interval is 0.12-0.14 sec. There is partial inversion of T_1, while T_2 is iso-electric (Fig. 10).

Additional electrocardiograms were taken on the day of the patient's death which occurred at 3:00 P.M. Records were taken at 10:41 A.M., 10:47 A.M., 11:04 A.M., 11:45 A.M., 1:25 P.M., 1:35 P.M., and 2:15 P.M. These all resemble the record of the previous day. The rate remains rapid, occasional auricular extrasystoles are seen, and there is no change in voltage or in conduction (Fig. 11 *A*).

The next electrocardiogram was begun at 2:55 P.M. which was five minutes before clinical death. In the forty minutes since the previous record the rate has become much slower—about 70 per minute (Fig. 11 *B*). The rhythm is regular and the sino-auricular node continues

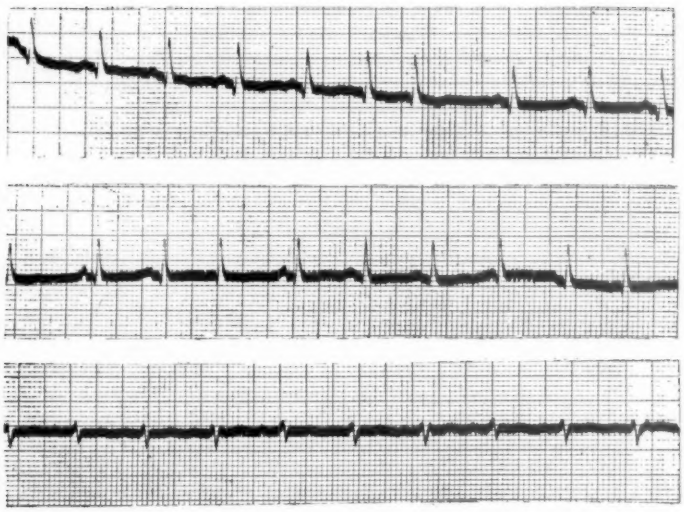

Fig. 10.—Case 5. Leads I, II, and III. About twenty-four hours before death.

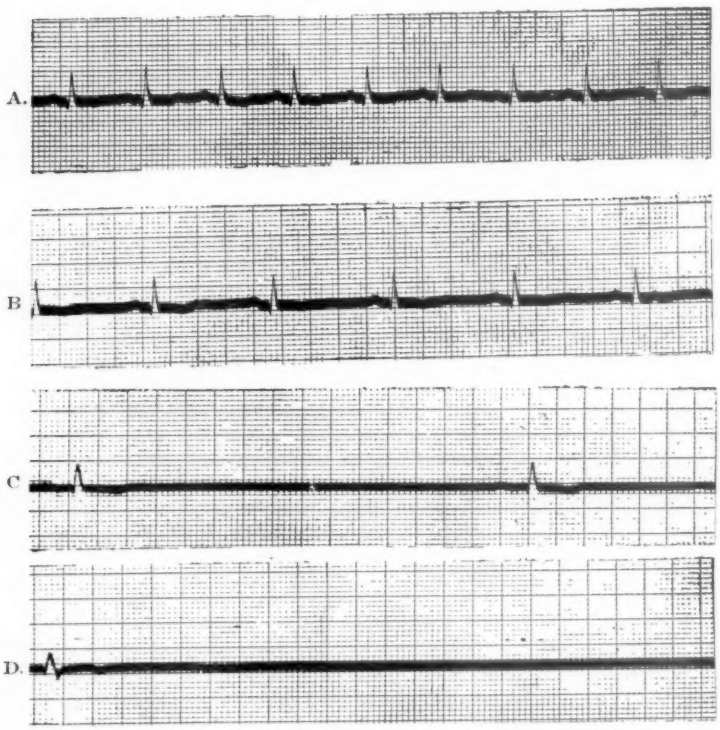

Fig. 11.—Case 5. Lead II. *A*, Taken at 2:15 P.M., about forty-five minutes before death. *B*, Four to five minutes before death. *C*, One minute after death. *D*, End of cardiac activity.

as the pacemaker. The P-R interval is still about 0.14 sec. Rare auricular extrasystoles are seen. At about this time clinical death occurred.

The record (Lead II) was resumed about a minute after death. The rate has now fallen to forty at the beginning of the record and grows gradually slower within the space of about ten seconds (Fig. 11 *C*). The P-waves at the beginning are upright. The conduction time is 0.24 sec. The R-wave is slurred, and the T-wave is inverted. As the rate slows, the P-waves diminish in amplitude and there seems to be a lengthening of the P-R interval, although this is very difficult to measure. Gradual slowing of the rate continues. Finally, after a series of beats coming quite regularly about three seconds apart, the heart stops beating for seventeen seconds, whereupon a single bizarre complex, probably of ventricular origin, is seen. Another pause of three or four seconds occurs, and cardiac activity is terminated by another bizarre complex (Fig. 11 *D*).

DISCUSSION

Electrocardiographic observations on the death of the human heart have been reported in sixty-five cases. To these the present series of five cases is added bringing the total to seventy. The three cases reported by Rohmer,[2] the twenty mentioned by Schellong,[6] and two of the six included in Willius' paper[7] are not susceptible to analysis because of insufficient data. This leaves forty-five cases that are reported in considerable detail.

There is a great variation in the mechanism of death of the human heart. This is the predominant impression that is to be gathered from a review of the cases reported in the literature. A conspicuous slowing of rate just before death is probably the most common finding. This is often associated with a change from normal sinus rhythm to an A-V nodal rhythm, but may occur without a change in the site of impulse formation. Marked slowing appeared in at least 70 per cent of the reported cases in which enough of the pertinent details were included. This figure is probably too conservative and would be larger if more data were given in the remainder of the cases. An excellent illustration of this decrease in rate is afforded by Case 5 in our series. Of nearly the same incidence (70 per cent) is the establishment of an A-V nodal or an idioventricular rhythm. However, aside from the slowing of the rate and the appearance of an A-V nodal rhythm, no other mechanism occurs sufficiently often to be predicted in a given case.

It is a common belief that ventricular fibrillation is the terminal mechanism in the majority of cases but this is not borne out by the electrocardiographic evidence. In about 20 per cent of forty-five cases ventricular fibrillation was the terminal event. In at least four other cases ventricular fibrillation was noted as a transient phenomenon. One

reason for the comparative infrequency of this finding may well be the fact that patients with ventricular fibrillation probably die suddenly in the majority of instances, whereas it is the cases with more gradual death that are susceptible to graphic study.

The age of the patient seems to play no part in determining the type of mechanism of the dying heart. Among the forty-five cases analyzed the age range is from nine months to eighty years. About 55 per cent were under forty years of age at the time of death. This group differed in no wise from the older patients in the types of terminal mechanisms recorded. From the data given, twenty of the forty-five patients may be classified as cardiac cases while the remaining twenty-five individuals died of causes other than heart disease. The mechanism of death in the two groups, divided on this basis, again shows no apparent difference. These facts have already been pointed out by Willius.[11] In other words, so far as the electrocardiographic manifestations during clinical death are concerned, it makes no difference whether the case be one of a child dying as the result of a pneumonia, or an old man dying because of a failing myocardium.

In order to make clinical application of our knowledge concerning the mode of cardiac death it is important not only to be able to recognize significant changes in the cardiac mechanism when they appear, but also to find these changes sufficiently in advance of death to afford an opportunity to apply therapeutic measures. An electrocardiogram is not needed to predict the death of the patient. It was obvious clinically, in most of the cases that have been reported, that the patient was dying, and therapeutic measures had been instituted before the electrocardiographer arrived to record the beats of the dying heart. In a few reported cases it is possible to determine the time before death when significant electrocardiographic findings were noted. Usually we are told that "just before the patient died" certain changes appeared. In most instances, therefore, these changes seem to precede clinical death by only a few minutes. This is illustrated in the series reported by Martini and Sekell[10] who kept careful records of time relationships. In their first case, for example, tachycardia persisted up to five minutes before clinical death. Again, in the fifth case of the same series, the graphic records showed a tachycardia from four to six minutes before death with an A-V nodal rhythm appearing only a minute and a half *ante mortem*. In the fifth case in our series it was apparent that the patient was *in extremis* for nearly twenty-four hours. During the last five hours, death was expected momentarily. Yet the electrocardiogram did not show important changes until five minutes before clinical death. Hence it seems that the graphic record is of academic rather than of practical interest. Significant changes in the electrocardiograms appear so little ahead of death that the patient is usually dead before the film is developed.

SUMMARY

Sixty-five cases of electrocardiographic studies of the dying human heart reported in the literature are reviewed and five additional cases are recorded. Conspicuous slowing of the heart rate is the most frequent change in the mechanism of the heart which immediately precedes death. It has been found in over 70 per cent of the cases. Next in frequency is the appearance of an A-V nodal rhythm or an idioventricular rhythm. It is impossible to differentiate between the mechanism of cardiac death in patients with or without heart disease. The age of the patient likewise does not determine the manner in which the heart dies. Electrocardiographic studies of the dying human heart are, for the present at least, solely of academic value, as significant changes appear in the record only a very few minutes before clinical death.

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VENTRICULAR FIBRILLATION WITH CARDIAC RECOVERY, CAUSED BY CAROTID SINUS PRESSURE, IN A CASE OF AURICULAR FIBRILLATION*

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WHILE there are relatively few recorded clinical cases of ventricular fibrillation, this arrhythmia is often mentioned as the cause of death in various types of disease; electrocution, coronary disease, chloroform poisoning, auricular fibrillation, paroxysmal tachycardia, other types of arrhythmia, etc. H. E. Hering,[1] drawing inferences from the frequent sudden death of experimental animals due to ventricular fibrillation, believes this arrhythmia a cause of death in patients who die suddenly and in whom, on pathological examination, no significant abnormalities are found.

Several cases of ventricular fibrillation with cardiac recovery have been recorded and reported by Kerr and Bender,[2] Levine and Matton,[3] De Boer,[4] Robinson and Bredeck,[5] Hoffmann,[6] and Dock.[7]

The case reported below is of interest not only because an electrocardiographic curve was obtained which is interpreted as being ventricular fibrillation, but because this arrhythmia occurred while doing a carotid sinus pressure test. The onset and cardiac recovery are recorded.

Czermak[8] in 1866 described a slowing of the pulse rate caused by pressure over the right carotid artery and attributed this effect to a direct mechanical stimulation of the vagus. Hering,[9] in his epoch-making researches, showed that the slowing of the cardiac rate and fall in systemic blood pressure are caused by pressure upon, or increased pressure within, the carotid sinus, a fusiform dilatation of the first portion of the internal carotid artery as it leaves the common carotid artery. He demonstrated that the sinus nerve, a branch of the glossopharyngeal, inervating the carotid sinus, is the pathway for reflexes causing the heart rate and blood pressure changes. De Castro's[10] anatomical studies have corroborated Hering's conception of the inervation of the carotid sinus. He demonstrated that nerve filaments found in the sinus portion of the internal carotid artery only, joined nerve filaments arising in the carotid body, to make the intercarotid nerve of De Castro (sensory) which enters the central nervous system principally through the ninth cranial nerve and to some extent through the vagal root ganglion.

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Wenckebach has for many years used the "Vagusdruckversuch" in clinical medicine. The recent researches of C. Heymans[11, 12, 13] and his coworkers, however, instigated by Hering's observations showing the importance of the influence of carotid sinus and depressor reflexes, rather than cerebral blood pressure changes, upon blood pressure, cardiac rate and control of adrenalin secretion, foreshadow changes in our concept of those diseases which cause, or are caused by, changes in blood pressure, cardiac rate and adrenal secretion. These studies are bringing the carotid sinus pressure test into more general clinical use.

During the course of a study on the clinical significance of the various types of reaction to carotid sinus pressure, many interesting electrocardiographic tracings were obtained by us. The electrocardiographic curves described below were recorded, while doing carotid sinus pressure tests, from a patient with severe myocardial disease and auricular fibrillation with a slow ventricular rate.

CASE REPORT

G. R. Male; aged 58 years; business man; born in the United States. Date of examination, November 20, 1930.

Family History.—Mother died at the age of 54 years, apoplexy; father died at the age of 60 years, heart trouble. One brother and one sister died in early adult life of pulmonary tuberculosis; two sisters and two brothers are well.

Past History.—Whooping cough; diphtheria; scarlet fever. No history of rheumatic fever or any of its manifestations. Married. Wife has four children; no miscarriages. Pneumonia at 31 years and typhoid fever at 35 years. Has had attacks of migraine and extrasystolic sensations since childhood. Venereal disease denied.

Present History.—Since the spring of 1930 patient has had signs and symptoms of cardiac impairment, dyspnea on exertion, swelling of the ankles, and subsequently nocturia and slight nocturnal dyspneic attacks. For the past six months he complains of a sense of constriction and pressure in his chest, radiating to the back, on walking. He had been told one year ago that he had high blood pressure.

Physical Examination.—Moderately well nourished male. Weight 174 lb.; height 75 in. Eyes react to light and accommodation. Eye grounds show retinal vessel sclerosis. Teeth—many extracted; pyorrhea alveolaris. No thyroid gland abnormalities. Chest—emphysematous; slight lateral curvature of the spine; occasional râles at both bases which clear up on deep breathing; no sacral edema. Temporal vessels tortuous and the walls palpable; radial vessel walls definitely thickened; brachial-vessel pulsations are visible. Heart—aortic configuration; left ventricle enlarged almost to the anterior axillary line; basilar vessel line is widened to the left; he has an auricular fibrillation with a slow ventricular rate. The highest systolic pressure was 180 and the lowest diastolic was 100 mm. Hg. A short blowing systolic murmur is heard at the apex; A-2 accentuated and musical; heart sounds poor and indistinct. Abdomen—rather prominent; liver enlarged two fingers below the costal margin. No fluid. Marked edema of the ankles, extremities otherwise normal; reflexes normal. Dorsalis pedis and posterior tibial pulsations present. Carotid sinus pressure on either the right or the left side causes a complete cardiac standstill during which time patient becomes extremely dizzy but not unconscious. At one time, however, he became bewildered for a short period. Fluoros-

copy:—Showed an aortic configuration with a very large left ventricle, a prominent aortic knob and a tortuous aorta; costophrenic sinuses are clear. Wassermann negative; uranalysis—trace of albumin, no sugar, specific gravity 1,020, urobilinogen present; blood chemistry normal.

Diagnosis.—Essential hypertension; coronary vessel sclerosis; myofibrosis cordis; cardiac decompensation; retinal and radial vessel sclerosis; auricular fibrillation; chronic bronchitis and emphysema.

Subsequent History.—Patient improved on rest, cardiac tonics and diuretics. Has had no subsequent attacks and is up and about at the time of this report.

Electrocardiographic Studies.—(Taken on the day of examination.) Fig. 1 shows an auricular fibrillation with an average ventricular rate of 66. Left axis deviation. In Lead I the R-T interval is depressed

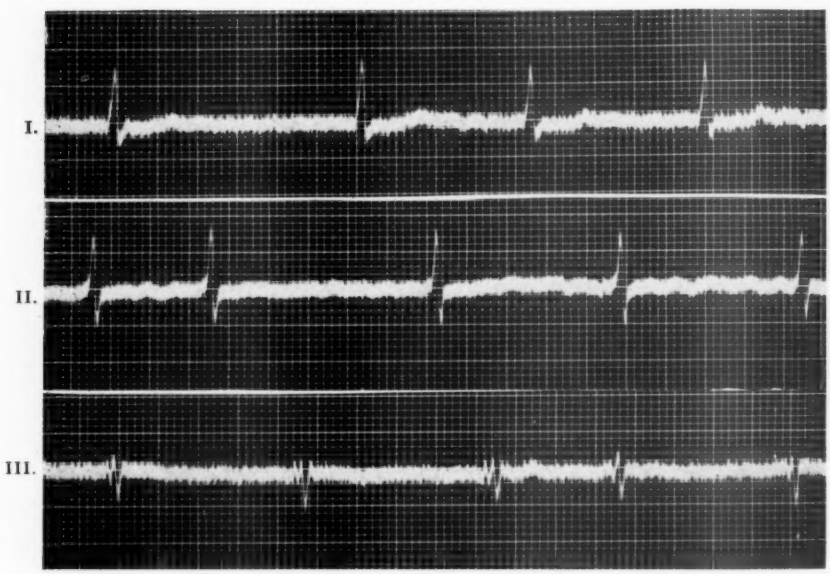

Fig. 1.—Auricular fibrillation, average ventricular rate 66. T-wave changes and slurring of the main deflections indicative of myocardial involvement.

below the isoelectric line. In Leads II and III the T-waves are isoelectric. The main deflections in all leads are slightly slurred.

Reaction to Carotid Sheath Pressure.—Fig. 2 (Lead III) shows the effect of left carotid sinus pressure. An absence of supraventricular complexes for a period of 8.68 seconds is noted. This period is interrupted by two aberrant ventricular complexes, one coming after a period of cardiac inactivity of 2.92 seconds and the other one following after 3.68 seconds. The aberrant ventricular complexes may be either right bundle-branch block or, more likely, ventricular extrasystoles. In the long periods of ventricular inactivity there is no change in conformation of the isoelectric line.

Fig. 3 (Lead III) was obtained as pressure was exerted upon the right carotid sinus. The S-wave is of low voltage and is the main de-

flection; auricular fibrillation is present. Carotid sinus pressure is made at the arrow; almost immediately following is a series of irregular movements of the isoelectric line at slightly varying rates, approximately 225 per minute. The first few complexes look like aberrant ventricular beats (A-B) and are similar in shape and direction to extrasystoles arising at the base of the ventricle. Then follows a period (B-C) of irregular movements of the isoelectric line showing no definite ventricular conformations. This is subsequently followed by a series of regular undulations of wider amplitude (C-D) and similar in shape and direction to extrasystoles arising at the apex of the left ventricle. A return to the original status, auricular fibrilla-

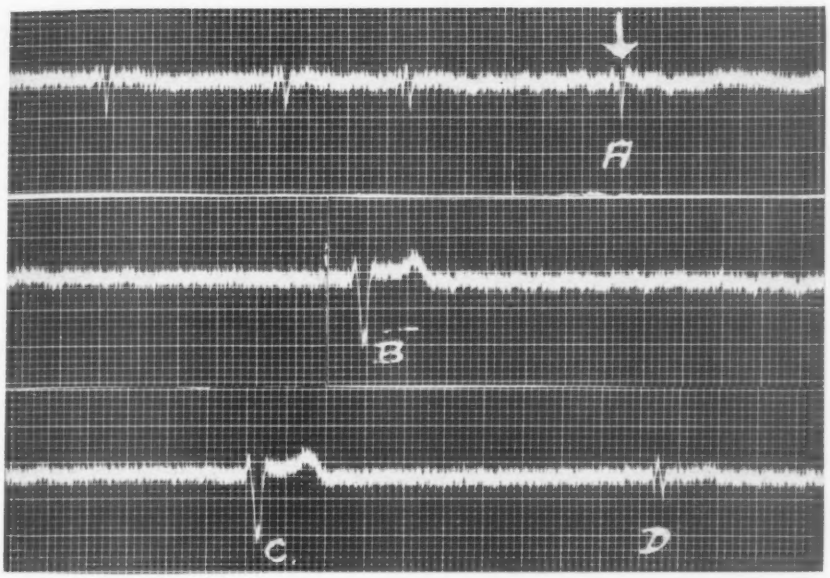

Fig. 2.—These are continuous strips of Lead III showing long pauses and aberrant ventricular complexes caused by pressure on the left carotid sinus (arrow). Time between supraventricular beats "A" and "D" is 8.68 seconds; between "A" and aberrant ventricular beat "B" is 2.92 seconds, and between "B" and aberrant beat "C" is 3.68 seconds.

tion, is now seen. This period of irregularity extends over a period of 8.68 seconds. Occasional complexes are seen which appear to be sinus beats (S). These complexes are not preceded or followed by pauses. No isoelectric period is seen in the tracing from "A" to "D."

During this time the patient became very dizzy, was bewildered for a few seconds and then became normal again.

DISCUSSION

A proper discussion and evaluation of the above findings necessitate answering the following questions: 1. Does carotid sinus pressure cause a reflex vagal stimulation? 2. Does carotid sinus pressure cause

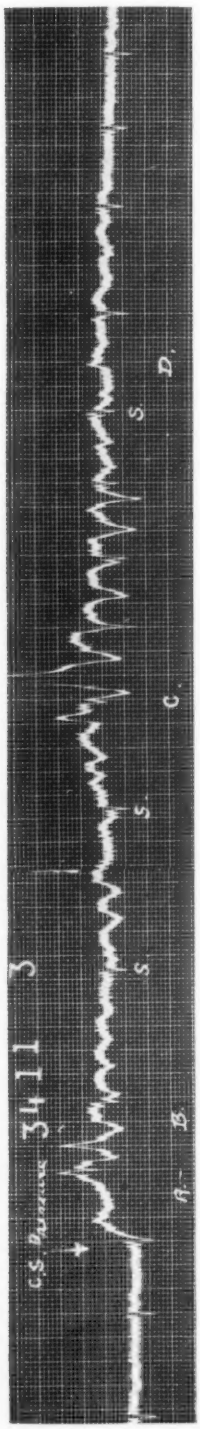

Fig. 3.—This arrhythmia was caused by pressure on the right carotid sinus (arrow). A-B and C-D are periods of ventricular activity which appear like successions of aberrant ventricular beats arising at the base and at the apex respectively. B-C is similar to Halsey's tracing of ventricular fibrillation. "S" indicates possible supraventricular complexes.

ventricular rate changes in auricular fibrillation, since in this arrhythmia the sinus is not the pacemaker? 3. What effect has vagal stimulation upon lower automatic centers in ventricular musculature? 4. Does Fig. 3 represent ventricular fibrillation?

1. Hering's and Heymans' investigations, as well as De Castro's anatomical studies, have shown that compression of the carotid sinus causes a reflex vagal stimulation.

2. Kronecker and Spallitta[14] in 1905, showed, in animals, that vagal stimulation slows the ventricular rate during auricular fibrillation. Robinson,[15] Fahrenkamp,[16] and Semerau,[17] and others have caused a ventricular slowing in patients with auricular fibrillation by pressure on the carotid sheath. Boas[18] by means of his tachometer, has shown that the ventricular rate in patients with auricular fibrillation is influenced by the same factors which influence ventricular rates in normal individuals, i.e., rest, sleep, excitement, etc. The slowing of the ventricular rate by carotid sinus pressure is due to the reflex stimulation of that part of the vagal mechanism which has its preponderant influence upon the A-V connecting system. By depressing the conductivity of the bundle it decreases the number of impulses conducted to the ventricle. Changes in cardiac rate in normal individuals are dependent upon changes in tone of the vagus and sympathetic which control the rate of impulse formation in the sinus.

3. While fibers of the sympathetic system are known to exist in all parts of the heart muscle, definite proof of the presence of vagus fibers in the ventricular musculature has not been forthcoming. Drury[19] has shown that vagal stimulation does not decrease the refractory period of ventricular musculature in experimental animals, and Lewis[20] states that the vagus has little effect on ventricular musculature. Rothberger and Winterberg[21] have shown that the fibrillation rate in the ventricle is not influenced by vagal stimulation.

On the other hand, both Hering[1] and Winterberg[22] were of the opinion that stimulation of the vagus caused lower ventricular centers to become hyper-irritable only indirectly; that its action was that of furthering only the occurrence of these arrhythmias. Hering[1] maintains that vagal stimulation depresses the force of ventricular contractions as well as conduction through ventricular musculature.

Hering[1] further states that not only electrical vagal stimulation, but vagal stimulation by breathing, etc., reflexly from the carotid sinus, from mucous membranes, etc., have the same influence upon ventricular musculature. Smith and Moody[23] reported cases in which premature contractions and idioventricular rhythms were induced by forced breathing.

Knoll[24] in 1897 caused all sorts of ventricular arrhythmias by vagal stimulation, including ventricular fibrillation, in curarized rabbit hearts. Rothberger and Winterberg[21] have, by vagal stimulation,

caused similar arrhythmias in dogs and cats which were previously administered barium chloride, chloroform and other drugs. Scherf,[25] by stimulating the right vagus, caused many ventricular extrasystoles and other aberrant ventricular arrhythmias in dogs to whom aconitine had been administered.

Kisch[26] in 1921 produced in animals a greater tendency to heterotopic ventricular arrhythmias by clamping both carotids. Many ectopic ventricular rhythms have been recorded by us (to be reported) and by others while doing the carotid sinus pressure test. It is found that these arrhythmias occur more readily in patients who have severely damaged ventricular musculature. Digitalis causes idioventricular rhythms, especially in persons with diseased heart musele. Latent bigeminal rhythms in well digitalized patients are sometimes brought out by carotid sinus pressure.

All these data seem to justify the impression that while normal ventricular musculature appears not to respond to vagal stimulation, diseased ventricular musculature, diseased by whatever cause, does respond to such stimulation by all sorts of ectopic idioventricular rhythms.

Braun and Samet[27] have shown that the effect of carotid sinus pressure, was markedly increased in cats, when branches, particularly of the left coronary arterial system, were tied.

It seems that a vicious circle is established in patients with severe myocardial disease, for not only does diseased ventricular musculature respond by the occurrence of idioventricular rhythms to vagal stimulation, but, as Braun and Samet have shown, and as has been noticed in the clinic, damage of ventricular musculature increases the irritability of the vagus.

4. The curves of ventricular fibrillation recorded, obtained both from experimental animals and human beings, are of various types. They seem to have the same relationship to each other, as do the various types of the auricular circuit movement arrhythmias, i.e., auricular flutter, with its regular auricular contractions at the rates of approximately 300 per minute; impure flutter or coarse fibrillation at higher and irregular auricular rates; and auricular fibrillation with its very high fibrillation rate, marked irregularity, dilatation of the auricle, and failure of coordinated auricular contractions. De Boer[4] and Rothberger and Winterberg[21] have described these various types of ventricular fibrillation. Lewis[20] has described various stages of ventricular fibrillation in experimental animals. The early stage of frequent premature ventricular contractions, followed by the stage of more or less regular movements of the isoelectric line (up to this time no dilatation of the ventricle has taken place), and finally tremen-

dously increased irregular ventricular circuit movement rates with a dilatation of the ventricle and an absence of coordinated ventricular contractions.

It seems to us that the curves of ventricular fibrillation described as flutter and impure flutter are really aborted stages of what ultimately might have been that stage of ventricular fibrillation which parallels auricular fibrillation. These stages or aborted types, if we may use that term, are exemplified by the following curves—the flutter stage or type, by Kerr and Bender's[2] first portion of Fig. 8; Dock's[7] curves, Fig. 2; De Boer's[4] and Hoffmann's,[6] etc.; and the impure flutter stage, by our Fig. 3. The fibrillation stage is exemplified by Kerr and Bender's[2] Fig. 9. Lewis characterizes Hoffmann's tracing and others like it as potential ventricular fibrillation.

In the auricular-circuit-movement arrhythmias transition from one type to another are not infrequent, particularly when quinine or digitalis has been given. There seems to be a greater tendency of transition from one stage or type to another in the ventricular circuit movement arrhythmias.

Fig. 3, at the onset (A-B) and toward the end (C-D), is similar to Dock's[7] curves taken from a patient in whom syncopal attacks were induced by adrenalin; to De Boer's[4] taken from a patient with complete heart-block, and which he described as ventricular flutter and fibrillation, showing at times a short series of ventricular aberrant beats; to Hoffmann's[6] curve obtained at the end of an attack of paroxysmal tachycardia before the establishment of a sinus rhythm, which he called ventricular fibrillation and which Lewis calls potential ventricular fibrillation; and to the curves of Rothberger and Winterberg's[21] Plate V, Fig. 13-a, obtained from a dog. For a short distance (B-C) in our curve, the rapid irregular undulations of the isoelectric line are different from those seen in parts of the curve A-B and C-D. This part (B-C) of Fig. 3 is similar to Halsey's[28] curve obtained from a patient dying of pneumonia.

This arrhythmia begins with ventricular aberrant beats immediately following carotid sinus pressure, goes into a ventricular circuit movement, returns again to aberrant ventricular coordinated beats and then to the previous status. We think that this curve represents activity in the ventricle which parallels the auricular arrhythmia called impure flutter or coarse fibrillation in the auricle. It represents an aborted ventricular fibrillation.

It seems that this patient had all the possible factors necessary for the occurrence of an ectopic ventricular arrhythmia. He had suffered from migraine and had extrasystoles for many years; thus supplying the possible developmental factor. Wittgenstein[29] believes that the occurrence of aberrant rhythms, paroxysmal tachycardias, is an indication of an exudative diathesis. Patient developed a myofibrosis

cordis, supplying the myocardial disease factor, and an auricular fibrillation with a slow ventricular rate, not dependent upon digitalis—indicating some degree of organic A-V block—supplying the factor that Davis and Sprague[30] believe necessary for the occurrence of aberrant ventricular circuit movement rhythms.

All these underlying factors being present, carotid sinus pressure stimulating a vagal system made hyper-irritable by diseased ventricular musculature caused the aborted ventricular fibrillation.

SUMMARY

The occurrence of a ventricular fibrillation upon carotid sinus pressure with spontaneous cardiac recovery is reported in a patient with auricular fibrillation, who had signs and symptoms of severe myocardial degeneration.

The newer physiology of the carotid sinus pressure test and its relationship to clinical medicine are briefly mentioned. The pathological physiology of ventricular-rate changes by vagal stimulation in auricular fibrillation is described and the effect of vagal stimulation upon lower automatic centers in ventricular musculature is discussed.

It is suggested that the occurrence of ventricular fibrillation in this patient is additional evidence in support of the concept that vagal stimulation, from whatever cause, will produce idioventricular arrhythmias in diseased ventricular musculature.

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UNUSUAL VARIATIONS OF THE ROENTGEN SHADOW OF THE ELONGATED THORACIC AORTA

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INTRODUCTION

THE x-ray appearance of the tortuous aorta is well known. In the anteroposterior view the supracardiac shadow is widened on both sides. The intersection between the right auricular border and the ascending portion of the aorta is rather low. The latter is more prominent, its outline being more curved than usual. On the left, the aortic knob is highly situated and prominent. Its shape and size depend upon the further course of the descending aorta; this vessel may be situated anteriorly to the vertebral bodies or more to their left. In the latter case, the descending aorta is unusually well visualized and may disappear behind the heart shadow in the region of the auriculoventricular junction and not as usually within the conus pulmonalis. The outline of this descending vessel is either straight or slightly curved, the convexity being directed to the left. In films taken with higher voltage and sufficient exposure or in films where the Potter-Bucky diaphragm is used, the shadow of the descending aorta is easily seen through the heart shadow and is always seen partly to the left of the midline. In the left anterior oblique position the entire loop of the aorta is seen, and the type of curve resembles rather more that of a circle than that of an ellipse or of an even more sharply kinked curve as we see it in normal conditions, but the circumference of the curve always remains smoothly outlined. In the right anterior oblique position there is no very characteristic picture, part of the descending aorta or sometimes the entire vessel being seen within the retrocardiac space. This type of aorta is found usually, although not always, in old people and in patients with arteriosclerosis and hypertension.

CASE REPORTS

In the following four cases of arteriosclerosis an unusual course of the descending aorta has been observed.

CASE 1.—The first case, Massachusetts General Hospital, X-ray No. 66530, June 20, 1927, was a carpenter, 60 years of age. He had suffered for years from an

arthritic condition of the knee. There were no other complaints. The Wassermann reaction was repeatedly positive. X-ray examination showed definite calcification of the popliteal artery on each side. The caliber of the left popliteal artery was about three times the normal—probably due to an aneurysm. Clinical examination revealed essentially normal heart findings. The aortic second sound was accentuated. The blood pressure was 160 millimeters of mercury systolic and 95 millimeters diastolic.

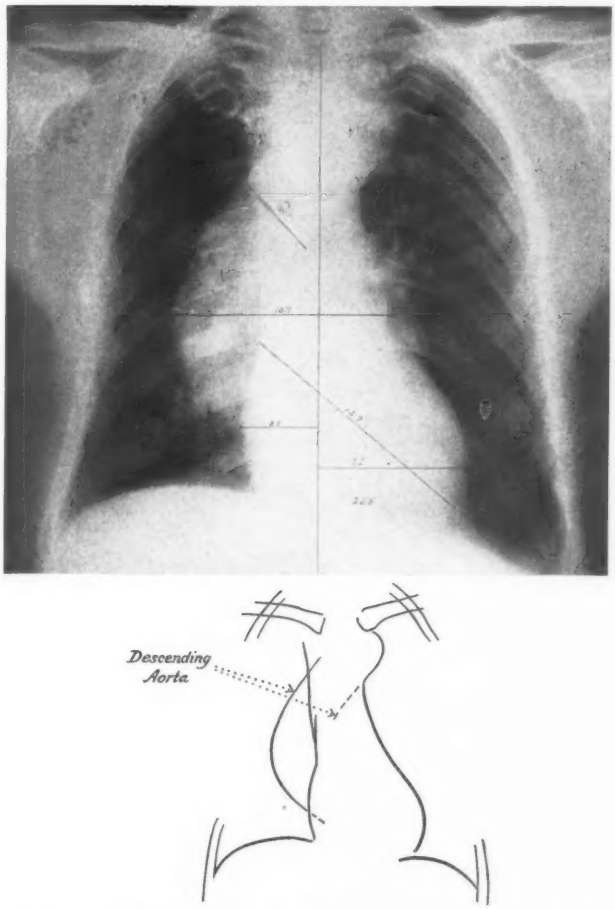


Figure 1—Roentgenogram, anteroposterior view, Case 1.

An x-ray film of the chest, anteroposterior view (Fig. 1), showed the heart to be normal in size and shape (transverse diameter 11 cm., internal diameter of chest 25.5 cm.). The supracardiac shadow was markedly enlarged, measuring 10.7 cm. The aortic knob was high to the left. The descending aorta turned in its course sharply toward the median line, its left contour being well seen, crossing the vertebrae into the right lung field. Its contour can be followed downward and medially to disappear within the right auricular shadow. In the right

anterior oblique view (Fig. 2) the trachea is seen to be displaced forward at the height of the aortic arch.

It is obvious that the aortic shadow seen in the anteroposterior view in the right lung field was caused by the descending aorta. This vessel shows a marked S-like curve directed posteriorly and to the right

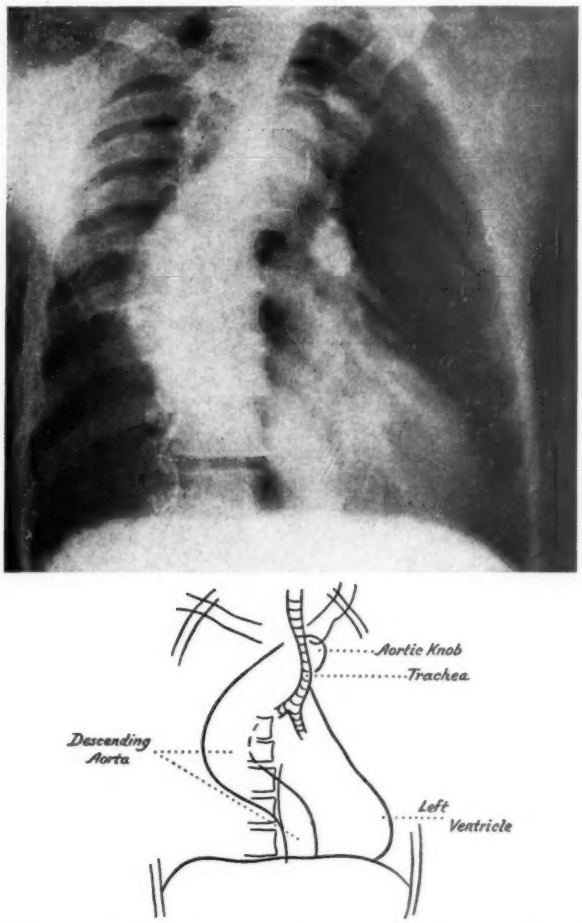


Figure 2-Roentgenogram, right anterior oblique view, Case 1.

in its upper part and forward and to the left in its lower part. The anterior and posterior portions are well visualized. The distinctness of the shadow makes it possible to establish a correct measurement of the width of the aorta: 5 cm. for the upper portion and 4 cm. for the lower. The right oblique view shows no shadow of the descending aorta overlying the vertebrae. Anteriorly in this view, the normal rather flat curved border of the ascending aorta is seen. The course of the aortic vessel can therefore be described as follows: The ascend-

ing aorta and arch are relatively normal. The descending aorta crosses the midline, thus displacing the trachea forward, bulges broadly into the posterior right lung field, and returns behind the heart to the midline.

Two findings are remarkable. First, the displacement of the trachea anteriorly has been known up to the present to occur with one

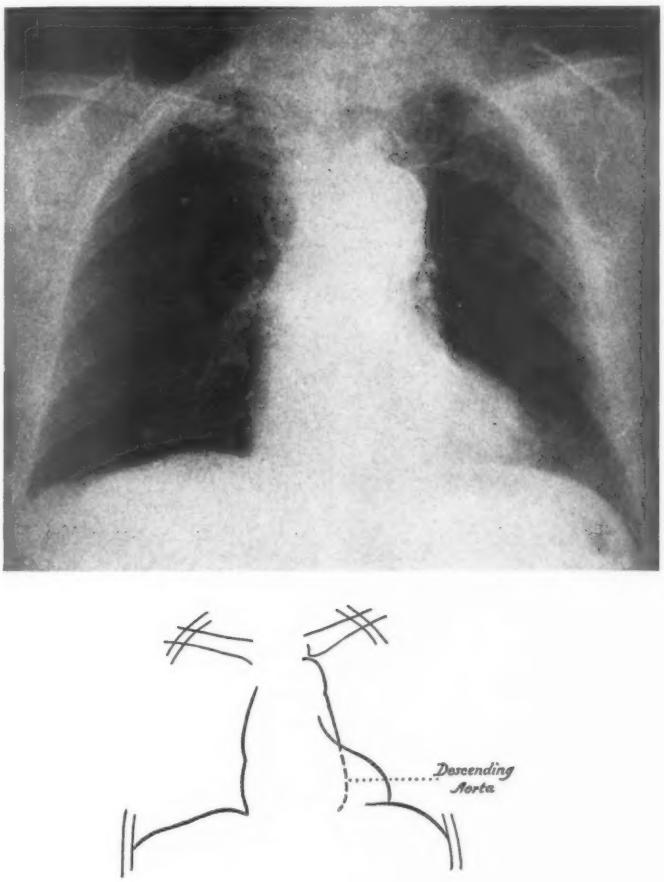


Figure 3 ~ Roentgenogram, anteroposterior view. Case 2.

other condition only, namely, the right sided aortic arch. With that congenital anomaly, the aortic arch turns behind the trachea and esophagus to the right of the midline. All cases of that anomaly which have been studied, however, have shown a very characteristic finding, the absence of the aortic knob on the left and a displacement of the trachea to the left at the height of the aortic arch. Neither of these findings is present in our case. Therefore, the diagnosis of this anomaly has to be discarded.

Second, the degree of curvature of the descending aorta is striking. One must assume that the left intercostal arteries have undergone a considerable lengthening. In using only the anterior view one might be tempted to diagnose an aneurysm of the ascending portion of the aorta. The best explanation for the abnormal course of the aorta is

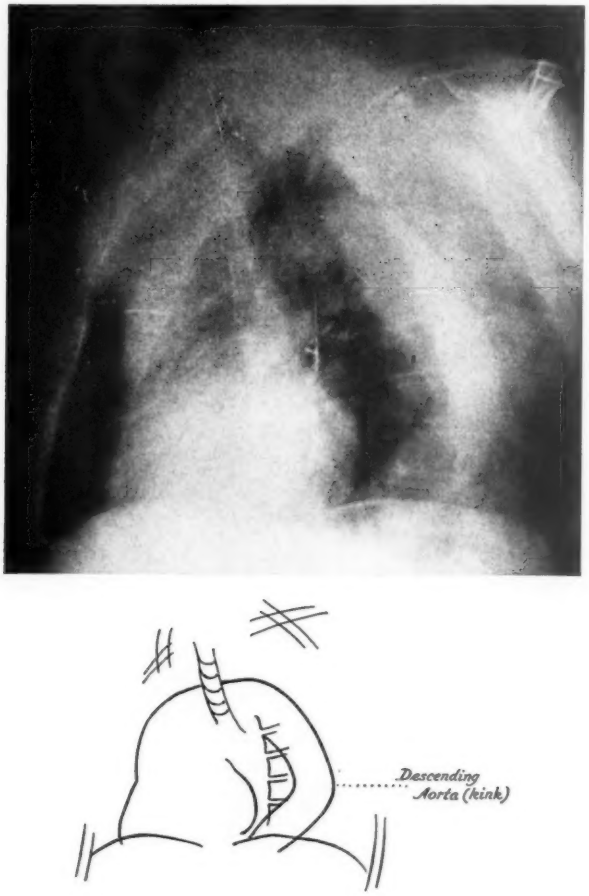


Figure 4—Roentgenogram, left anterior oblique view, Case 2.

the conception that the vessel has become too long between its two points of fixation, the heart and the diaphragm. We know that the process of arteriosclerosis affects chiefly the descending portion of the aorta. Syphilis, though present in this case, cannot account for the aortic anomaly.

CASE 2.—The second case, Massachusetts General Hospital, X-ray No. 132754, January 29, 1931, was a male, 61 years old, who worked as a butler. Fourteen years before, a diagnosis of early tabes was made. The Wassermann reaction was repeatedly positive. He suffered from attacks of shooting girdle pain. There were

no complaints suggesting heart disease. Some years before the date noted above, the heart findings had been essentially negative. The only abnormal circulatory finding that had developed since was slight hypertension, the systolic blood pressure being 160 millimeters of mercury.

In an x-ray of the chest, anteroposterior view (Fig. 3), the heart showed an "aortic configuration" but its size was within the limits of

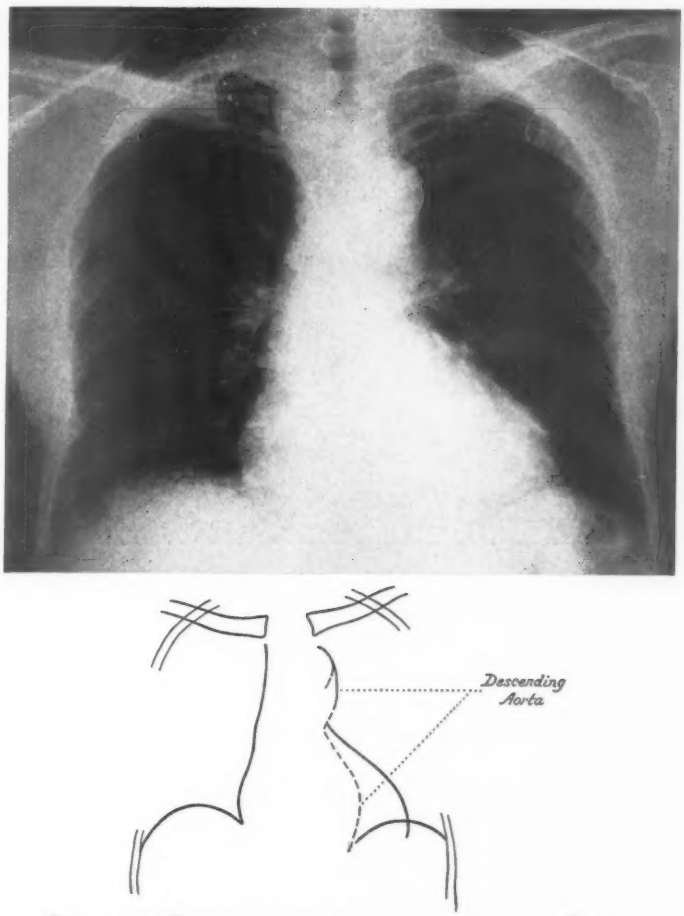


Figure 5 ~ Roentgenogram, anteroposterior view; Case 3.

normal (transverse diameter 13.8 cm., internal thoracic diameter 30 cm.). The aortic shadow was moderately widened and showed calcification. Its course is seen through the heart shadow as it curves medially above the diaphragm. In the left anterior oblique view (Fig. 4) the descending aorta is well seen in its entire course as a rather dense band of about 3.7 cm. in diameter. Its upper two-thirds are directed downward and slightly backward, its lower third markedly forward, thus forming a kink. In the anteroposterior view only, it would be

difficult to differentiate this abnormality from a fusiform aneurysm of the lower portion of the descending aorta, an appearance which the oblique view conclusively demonstrates as being due to the wide course of the aorta. This aortic deformity is explained by elongation of the aorta, so that kinking is necessary to allow it to fit into the

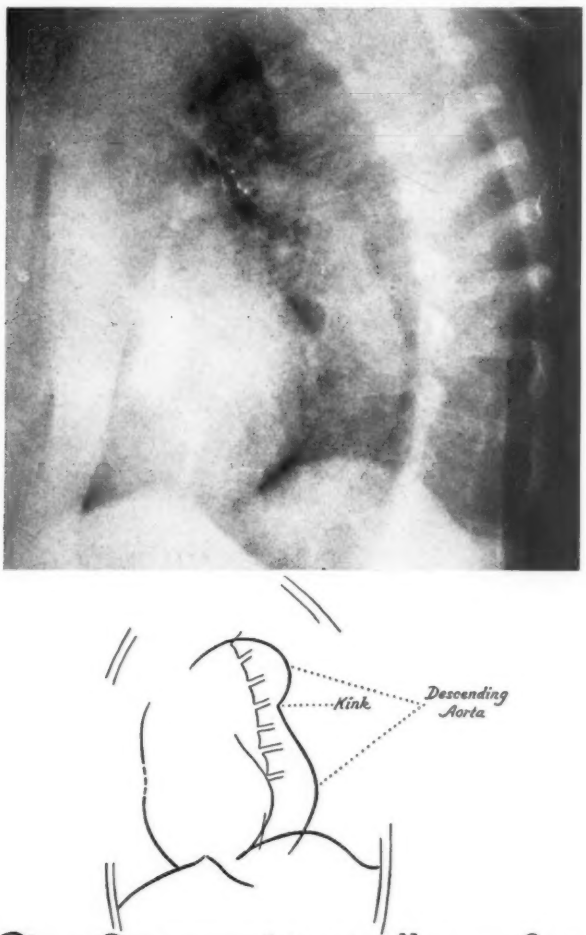
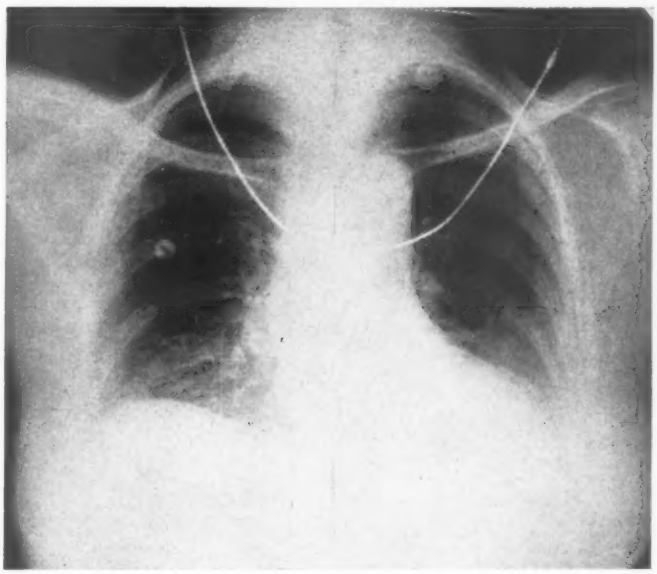


Figure 6—Roentgenogram, left anterior oblique view, Case 3.

thorax. Atherosclerosis causes such elongation; luetic aortitis may or may not be a factor underlying the atherosclerosis.

CASE 3.—The third case, Massachusetts General Hospital, X-ray No. 189542, December 13, 1930, was a male, 50 years old, who worked as a carpenter. For six months he had been suffering from headache, vertigo, and transitory scotomas. The heart was slightly enlarged to the left. The aortic second sound was accentuated. The blood pressure was 220 mm. mercury systolic and 118 mm. diastolic, later 170 mm. systolic and 90 mm. diastolic. The Wassermann reaction was negative. The radial and brachial arteries were tortuous. There were no clinical signs of coaretation of the aorta. The diagnosis was essential hypertension.

In an x-ray film of the chest, anteroposterior view (Fig. 5), the heart shows an aortic configuration and moderate enlargement (transverse diameter 16 cm., internal thoracic diameter 30.7 cm.). The aortic knob is prominent. The left border of the descending aorta below the aortic knob bulges considerably. Below the level of the left bron-



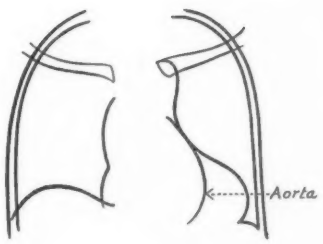


Figure 7—Roentgenogram, anteroposterior view. Case 4.

chus within the heart shadow, there is a definite indentation. In the left anterior oblique view (Fig. 6) at the upper portion of the descending aorta below the arch, the outer border of the aortic shadow shows a marked indentation, the course of the entire vessel undergoing a sudden change in direction. In the absence of a well defined anterior border in almost the entire course of the aorta, no measurement can be made, but for a short distance above the diaphragm where the anterior border is visible, the aorta shows narrowing in its downward course and some calcification is seen. In this case, the indentation below the aortic

arch best seen in the oblique view might suggest a real narrowing such as is present in coarctation of the aorta. The lower margins of the posterior ribs, however, do not show the erosions seen in this disease and no clinical evidence of this anomaly is present. As the inner and anterior contour of the lower portion of the descending aorta could

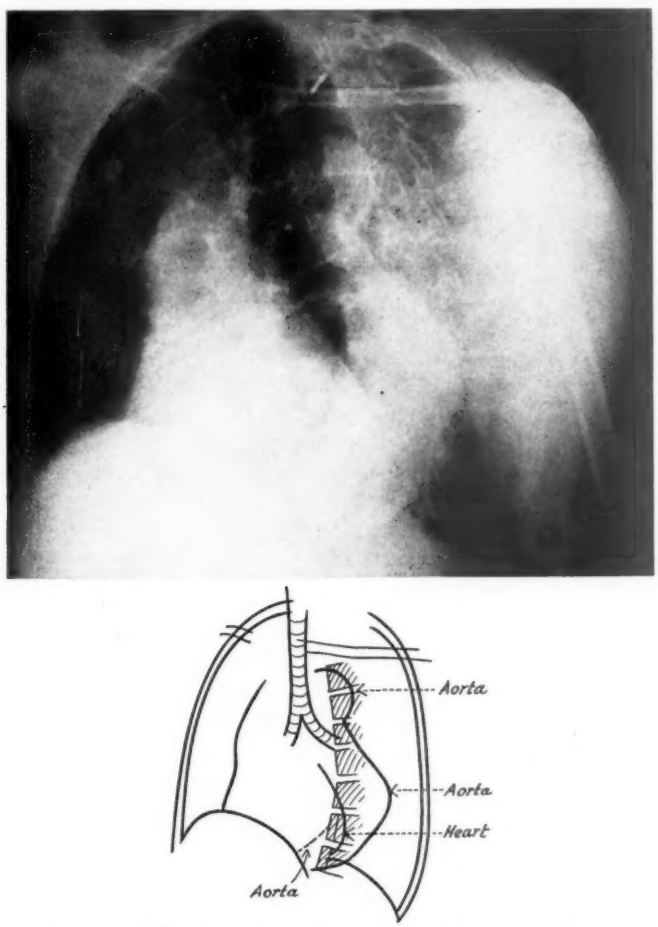


Figure 8—Roentgenogram, left anterior oblique view. Case 4.

not be visualized, dilatation cannot be excluded, but clinically and serologically no evidence of luetic aortitis or aneurysm was present.

CASE 4.—The fourth case, Baker Memorial, Massachusetts General Hospital, X-ray No. 2176, March 10, 1931, was a woman 50 years old with osteomalacia. There had been a definite history of dietary insufficiency for a period of years. No parathyroid tumor was found. Her symptoms and signs consisted of pain in the back and hips with definite tenderness along the ribs and crests of the ilia with dorsal kyphosis. The Hinton (Wassermann) reaction was negative. The renal function test was normal. The nonprotein nitrogen in the blood was normal in amount, but the blood phosphorus was low. The Graham test was negative.

Physical examination was negative except for the condition of the bones. Her blood pressure was 140 mm. mercury systolic and 85 mm. diastolic. The x-ray finding of the kinked aorta was incidental in the course of routine examination.

The anteroposterior view of the heart shadow by x-ray (Fig. 7) shows moderate cardiac enlargement and a curved, well visualized, descending thoracic aorta which can be seen in its lower portion behind the shadow of the heart. The ascending aorta is tortuous also and the knob is prominent. The heart is moderately enlarged and transverse in position. In the left anterior oblique view (Fig. 8) there is quite clearly visible a kink in the aorta, rather high up, just below the origin of the great thoracic vessels. The aorta can be seen descending to the diaphragm behind the heart shadow.

There is no evidence of lues in this case and coarctation of the aorta can also be excluded.

SUMMARY

Four cases of arteriosclerosis, with or without hypertension or lues, are described in which unusual x-ray findings of the descending aorta were detected. One case showed the vessel situated far out in the right chest. Aneurysm of the ascending aorta had to be considered in the differential diagnosis. Forward displacement of the trachea in this connection constitutes a new observation.

The other three cases showed kinking in the course of the vessel; differential diagnosis of aneurysm of the descending aorta and of coarctation of the aorta had to be considered.

In all four cases the use of oblique views was of the greatest value. Abnormal lengthening of the aorta due to sclerosis and hypertension explains these findings.

We are indebted to the X-ray Department of the Massachusetts General Hospital, Dr. George W. Holmes, Director, for cordial assistance in studying these cases, and to Dr. Arlie V. Bock for permission to record his patient, Case 4.

THE SUBCLAVIAN PULSE IN AORTIC VALVE DISEASE*†

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DEFORMITY of the aortic orifice has long been known to alter the character of the arterial pulse. These variations from the normal were first studied clinically by palpation, later by the various types of mechanical sphygmographs, and recently by optical registration. The radial pulse has been carefully studied by clinical and instrumental methods and the results correlated.[1, 2] The subclavian pulse is a more desirable source of instrumental registration because of its large size and its nearness to the aorta. In addition the subclavian pulse contour is similar to that of the aortic pulse and is relatively free from changes in transmission. Optical registration permits not only the accurate study of contour changes but also the study of the dynamics of the heart in various valve lesions. In this way the findings in experimentally produced valve lesions may be correlated with the records of clinical cases. The clinical pulse in free aortic insufficiency may be distinguished from the pulse modified by varying degrees of stenosis. The records permit the study of the finer details of pulse contour and serve as an accurate check of clinical examination. In aortic insufficiency the water-hammer and collapsing features may be carefully analyzed.

Pure aortic insufficiency induced experimentally[3] in dogs produces a central (aortic) pulse curve of characteristic contour. The anacrotic rise is steep, and systolic vibrations are often superimposed on the top of the curve, while the incisura is sharp and deep. The after vibrations are slight or lacking and the diastolic decline is rapid. Likewise the central pulse curves of experimental aortic stenosis[4] are of characteristic contour. The initial rise which is abrupt and is low on the anacrotic rise is followed by an incisura. The curve then rises slowly to its summit at the end of ejection with vibrations interrupting the rise. From experimental data one anticipates in free aortic insufficiency in man the following pulse characteristics: A large pulse with an interrupted rapid ascent cut by vibrations near the summit; the incisura deep and after vibrations slight or lacking; and a rapid diastolic decline. Likewise in clinical pulse curves of patients with aortic insufficiency modified by moderate stenosis some evidence of an

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†A brief report of this work was given at the meeting of the Central Society for Clinical Research, November 22, 1929.

anacrotic incisura should be found which is not displayed by the curves of uncomplicated aortic insufficiency while the incisura and diastolic fall should be less precipitous.

CLINICAL CASES

Ninety-four patients with accepted evidence of aortic valve deformity were studied, and in twenty-two instances pathological examinations were subsequently made. These cases were easily divided clinically into three groups: (1) those with evidence of free insufficiency (caused by syphilitic valvulitis and by acute and subacute bacterial endocarditis), thirty-five cases; (2) those with less free insufficiency and modified by varying degrees of stenosis (caused by healed rheumatic scars), forty-four cases; (3) those with frank signs of aortic stenosis (caused by rheumatic and arteriosclerotic scarring), fifteen cases. The central (subclavian) pulses in these clinical types were studied by optical

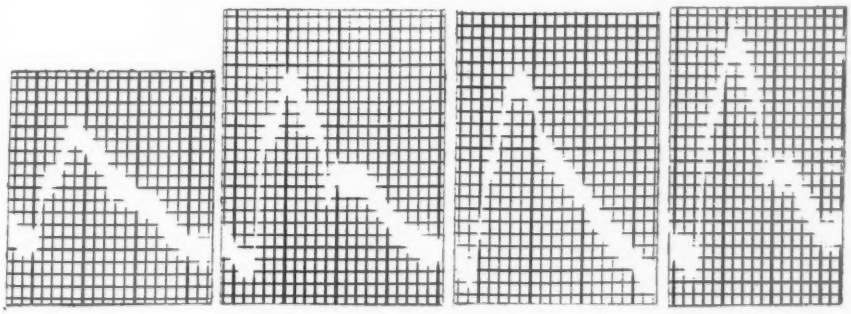

Fig. 1.—Normal subclavian pulse curves.

registration, and comparisons were made between the records and the clinical data.

Post-mortem examinations were made on twenty-two of the patients: (a) in six cases of rheumatic aortic insufficiency; (b) in fourteen cases of luetic aortic insufficiency; (c) in one case of aortic stenosis; and (d) in one case of subacute bacterial endocarditis with aortic insufficiency.

METHOD

Records were taken with a cup receiver firmly placed above the middle of the clavicle, the patient lying in the semirecumbent position. The Wigger's capsule was employed to inscribe the pressure changes photographically, with the electrocardiogram (Lead II). The curves were then enlarged uniformly and studied with regard to contour. In all instances immediate clinical observations of the subclavian pulsation were made by digital palpation. Notes were taken at the time of the registration and comparisons of the clinical data with the sphygmograms were made.

Representative normal records are illustrated in Fig. 1. The steep upstroke is caused by the ejection of blood into the aorta. This initial rapid rise completes from one-half to two-thirds of the anacrotus* and is followed by a more gradual rise to the top of the pulse. This summit may be sharp or rounded and is succeeded by a short and steep fall. Ejection terminates at the beginning of the incisura when ventricular diastole begins and there occurs a reverse movement of the blood column toward the aortic valves as they close. Following the incisura are several after vibrations which are simultaneous with the second sound. The curve then falls away gradually in diastole, broken in its descent by slight vibrations, due to the reflection of the pulse wave by the branching arterial tree.

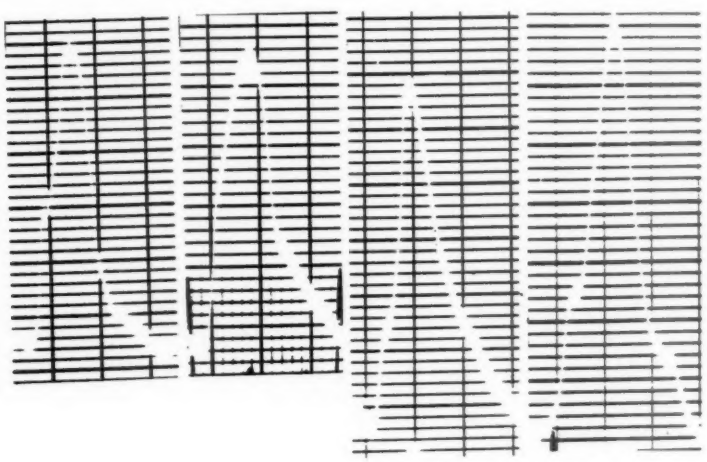

Fig. 2.—Subclavian curves from patients with aortic regurgitation caused by syphilis.

1. *Pure Aortic Insufficiency.*—Records were taken from patients with unmistakable clinical signs of free aortic insufficiency. Clinically, the radial pulse was large and typically Corrigan in quality. The rise was steep, the pulse top sharp and ill-sustained, and the fall rapid. The subclavian pulse was similar in its characteristics. Pulses like these were found most frequently in aortic insufficiency due to syphilitic pathological change and in acute and subacute bacterial endocarditis.

The recorded pulses (Fig. 2) show a sudden steep initial rise hesitating one-fourth to one-half the total height of the anacrotus.† The rise succeeding this interruption is almost equally rapid and terminates in a sharp peak, followed by a rapid catacrotus. Rarely are vibrations seen on the top of the inscribed records. The anacrotic

*As pointed out by Wiggers, the normal subclavian pulse frequently has this anacrotic interruption.

†Analysis of the curves shows that ejection causes this initial rise (not the pressure increase during the brief isometric period).

interruption is found lower down on the ascent than on either normal curves or on those of rheumatic aortic insufficiency. The bottom of the incisura is found after 0.7 of the catacrotus has been inscribed (in normals this figure was 0.3-0.5). The incisura thus is deeper and there is little evidence of an after vibration. These curves are characteristic, and in fourteen instances the diagnosis of luetic aortic disease was confirmed by autopsy. The lesion of syphilis as described

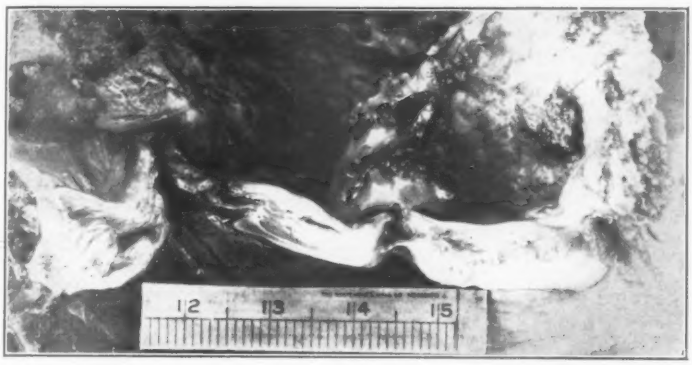

Fig. 3.—Aortic valve distorted by syphilitic changes.

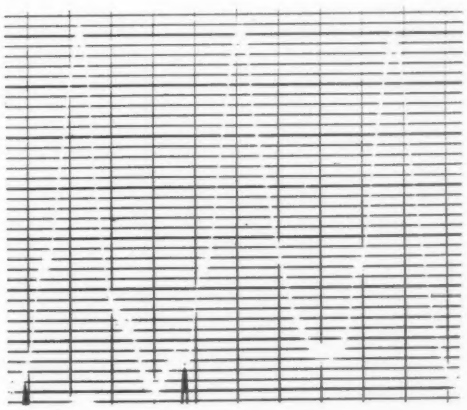

Fig. 4.—Subclavian pulse curve from patient whose aortic valve is illustrated in Fig. 3.

by Scott[5] begins in the aorta and involves the aortic leaflets first at the commissures. Later, the commissures are widened, the leaflets are deformed, and the ring is dilated. The pathological process results in relatively pure insufficiency of the valve, and the ejection of blood from the left ventricle is free and unobstructed. It is interesting to note that the pulse records differ from those obtained by Wiggers[3] in animals with experimental aortic insufficiency in that the experimental curves do not show the anacrotic interruption low on the ascent, but otherwise are similar. Fig. 3 shows the aortic valve of a patient who

had clinical evidence of free aortic regurgitation. The subclavian pulse was large and the summit was rapidly reached. The top of the pulse was poorly sustained and the catacrotus fell away rapidly. Dilatation of the ring, rolling of the leaflets, and separation of the leaflets is seen in the photograph. Fig. 4 is the subclavian pulse curve recorded from this patient and illustrates graphically the examiner's sensations.

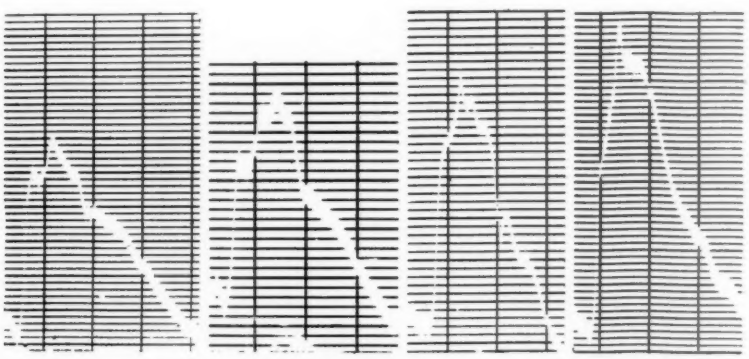

Fig. 5.—Subclavian curves from patients with aortic regurgitation caused by rheumatic process.

Fig. 6.—Aortic valve distorted by rheumatic changes.

2. *Curves of Aortic Insufficiency With Some Evidence of Stenosis.*—Curves were taken from young patients with a history of rheumatic fever and who had no evidence of syphilis. Clinically the subclavian pulses were Corrigan in quality and were felt to rise steeply and reached the summit near the end of the pulsation. At the top of the pulse which was sustained, vibrations were felt. The diastolic fall did not seem abnormally rapid or deep. These clinical impressions were confirmed by the graphic records (Fig. 5). The rapid rise is occasionally interrupted by a notch two-thirds the distance up the

ascent. The pulse continues to rise after the first steep ascent and the top of the pulse, which is usually cut by vibrations, is reached near the end of ejection. The drop to the incisura is steep but does not extend much farther than the normal and the diastolic portion of the curve falls away gradually. Following the incisura are slight after vibrations, lacking in some curves. These records are strikingly like experimental curves of this valve lesion. Post-mortem studies in rheumatic aortic insufficiency usually reveal varying degrees of stenosis. The aortic ring generally is not dilated and the leaflets are stiffened in their partially diastolic position. In addition they are adherent at their commissures. This is illustrated in Fig. 6 showing the aortic orifice of a patient aged twenty-one years with a rheumatic history and clinical signs of free insufficiency. The subclavian pulse was large, rose steeply, and was fairly well sustained. The graphic pulse curve (Fig. 7) showed the characteristics just described.

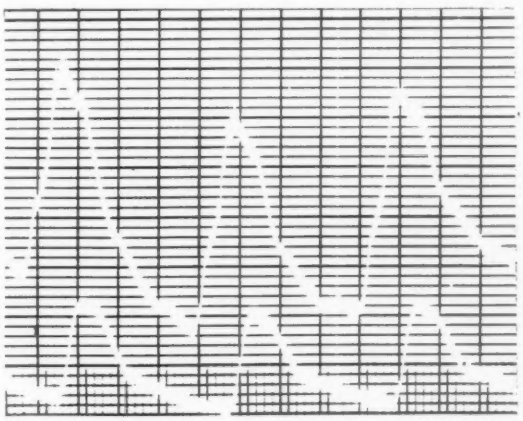

Fig. 7.—Subclavian pulse curve from patient whose aortic valve is illustrated in Fig. 6.

3. *Aortic Stenosis.*—Patients presenting the accepted clinical signs of advanced aortic stenosis were studied. The diagnostic criteria were as follows: Small volume pulses, anacrotic in quality, palpable systolic thrill and harsh systolic murmur over the aortic area, transmitted to the neck vessels; either a faint second sound was heard or a slight diastolic murmur. These patients all had subclavian pulses that were reduced in volume, slow in ascent, with the rise definitely interrupted by palpable vibrations. The patients had either rheumatic or arteriosclerotic scarring of the aortic orifice. The graphic records (Fig. 8) illustrate these sensations accurately and in addition show other features. The first rise is abrupt but brief and is terminated by a sharp peak. This is followed by an incisura. The succeeding rise is slow, is cut by vibrations, and ends in the summit of the pulse. The drop to the incisura is usually reached in 0.3 to 0.5 of the total fall, depending on the degree of the associated insufficiency, the wave then

falling away gradually in diastole. These clinical records may be compared with curves obtained in animals with experimental aortic stenosis[4] and exhibit striking similarity. The small amplitude of the pulse curve with a sharp initial rise, an anacrotic incisura relatively low on the upstroke, a slow ascent cut by vibrations, the rounded summit, the indefinite catacrotic incisura and gradual fall in diastole duplicate the picture found in the experimental curves.

Modifying changes in cardiodynamics in patients with aortic insufficiency produce curves preserving the general contour yet showing some variations:

1. Advanced failure. The pulse curves obtained from patients having the usual clinical evidence of aortic insufficiency and in addition signs of congestive failure presented a small pulse, Corrigan in quality. The subclavian curve showed the sudden and sharp anacrotus terminating in a sharp and ill-sustained peak, with a rapid diastolic

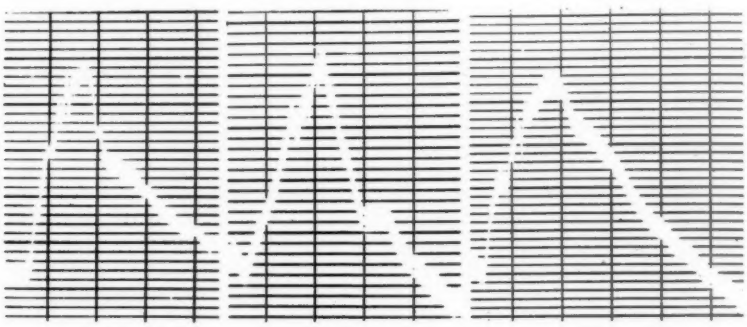

Fig. 8.—Subclavian curves from patients with aortic stenosis.

decline. This pulse although preserving the general contour seen in free insufficiency was reduced in size.

2. Bradycardia. The effect of slow rate was studied in a patient who in addition to free aortic insufficiency of luetic origin had complete heart-block with a ventricular rate of 40. The record showed an abrupt rise terminating in a relatively sharp summit and a rapid fall in diastole. Thus with a prolonged diastole and increased diastolic filling of the ventricle, sudden and rapid ejection took place which led to the conclusion that there could be little or no aortic obstruction. At post-mortem the typical changes of luetic aortitis with involvement of the aortic leaflets were found—the ring being considerably dilated.

3. Tachycardia. Curves with moderate tachycardia in patients with free insufficiency were typical of those found in free insufficiency, and in spite of the increase in rate the diastolic portion of the curves fell away rapidly. Curves recorded in the rheumatic aortic insufficiency group likewise were similar to those with slower rates.

DISCUSSION

Aortic Insufficiency.—Aortic regurgitation of luetic origin is comparable with the insufficiency experimentally produced because both lesions are relatively pure. The central pulse curves in the two while bearing considerable resemblance to one another are not identical in contour. The initial rise, in the clinical cases, terminating in an incisura, is due to the wide open orifice permitting the effective intraventricular pressure to be almost immediately transmitted to the aorta because the aorta and the left ventricle are in effect one chamber.* In clinical cases the aortic orifice is in addition dilated and often widely so. The aorta and large peripheral arteries are dilated, and this factor is an additional cause of the low diastolic pressure and reduced peripheral resistance. The experimental lesion produces an insufficient valve and may produce some dilatation of the aortic ring, but is not associated with the dilated peripheral arteries. The clinical curves in pure insufficiency show an anacrotic interruption low on the ascent while the experimental lesion produces curves rising steeply without this hesitation or notch.

What is the explanation for this difference in pulse contour? In the clinical curves the first part of ejection meets with little peripheral resistance, hence the sudden rise of the pulse curves. The hesitation or notch may represent the resistance caused by initial aortic filling. The subsequent rise of the pulse, while steep, is slower, due to the greater peripheral resistance offered by a partly filled aorta. The vibrations on the top of the experimental curves may be due to the vibrations of the aorta initiated by the sudden ejection of an augmented ventricular contents. These vibrations are slight or lacking in the clinical curves because of the damping effect of the dilated arteries.

The interruption in the anacrotic portion of the curve found low down on the curves of free insufficiency is lacking or is found higher up on the curves of rheumatic aortic insufficiency. These curves resemble more closely in their first portions the curves of experimental lesions. This concordance is due to the fact that the aortic ring is less dilated and in this more nearly approximates the experimental lesion. The catacrotic portion of the curves in clinical cases falls more steeply in pure insufficiency than in insufficiency modified by stenosis. Likewise the diastolic portion of the curve falls away more rapidly—both factors due no doubt to the freer ejection and the larger leak.

Aortic Stenosis.—The curves of aortic stenosis in clinical and experimental lesions resemble one another, although the almost constant

*Katz and Feil[8] showed that the isometric period is distinctly shortened in clinical cases of aortic regurgitation.

presence of some insufficiency in the clinical cases makes the two lesions not precisely comparable. The predominance of the stenotic lesion masks in a great measure the effect of the insufficiency in the clinical cases. This result of insufficiency is best seen in the catacrotic portion of the clinical curves—both in the fall in pressure during reduced ejection and in the diastolic portion of the curves.

SUMMARY

The subclavian pulse was studied in ninety-four patients with aortic valve disease. The curves of aortic insufficiency may be divided into two groups: (a) pure insufficiency, as caused by lues and by bac-

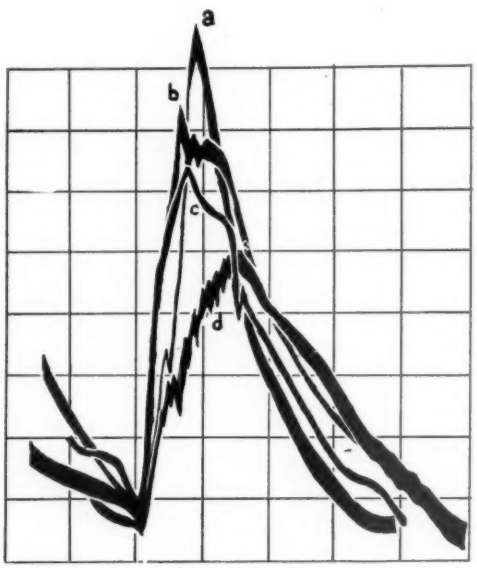

Fig. 9.—Superimposed subclavian curves in various types of aortic valve disease and normal control. See text.

terial endocarditis. These curves have been described and differ in some details from the experimental curves; (b) curves with some evidence of stenosis, found clinically usually in rheumatic cases. These curves more nearly resemble the experimental curves, especially in the anacrotic portions. The records of aortic stenosis are characteristic. Because they give evidence of the freedom of the insufficiency and the degree of the stenosis, subclavian pulse curves have diagnostic value in the differentiation of pure insufficiency from insufficiency modified by stenosis and in cases of aortic stenosis. Fig. 9 illustrates the various types of subclavian curves recorded in aortic valve deformity. The curves, traced from clinical records, are superimposed. Curve *c* is the normal control; *a* is from a case of free insufficiency of

luetic origin; *b* is from a case of aortic insufficiency with slight stenosis (rheumatic etiology); and *d* is a curve of stenosis. These records illustrate in a comparative way the various types.

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DIGITALIS DOSAGE IN AURICULAR FIBRILLATION

The Influence of the Activity of the Cardiac Nerves on the Size of the Effective Dose*

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DIGITALIS has been in common use for about a century and a half, and it would seem that after so many years little that is new could be added to our knowledge of its method of employ. Yet, as can be attested by every physician who sees a large number of patients with heart disease, many of the sick suffer needlessly and even die because they have received improper treatment with digitalis. In large part, of course, this is due to lack of application of existing knowledge, for Withering himself pointed out that enough of the drug must be given to produce a definite action, such as slowing of the pulse, diuresis, or vomiting.

In recent years, particularly in the United States, much attention has been directed to the standardization of digitalis preparations, and to the establishment of doses adjusted to the body weight of the patient, and to the speed of excretion of the drug. These studies have been valuable in improving the available preparations of digitalis, in encouraging more adequate dosage, and, in particular, in making possible quantitative investigations of digitalis administration. On the other hand, they have unfortunately led to a too rigid routine in the employment of the drug, and to a too implicit reliance on the dose as theoretically worked out, with a corresponding neglect of the clinical criteria of digitalis action. This schematization has arisen in spite of the fact that Eggleston in his original paper[1] reported that in 17 of 48 cases, doses of digitalis much larger than the average were given without the production of more than mild toxic symptoms. Mackenzie and many German observers have repeatedly emphasized the differences in susceptibility of individuals to digitalis. No adequate explanation has been offered for these varying degrees of tolerance to the drug.

In a previous communication[2] I again drew attention to the lability of the ventricular rate in patients with auricular fibrillation who were under the influence of digitalis, and pointed out that alterations in rate are governed by neurogenically determined changes in conductivity of the specific conducting tissue of the heart. The ventricular rate in these patients is therefore largely controlled by the cardiac

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nerves. It was further shown that patients with auricular fibrillation and labile ventricular rates, are, as a rule, high strung and nervous, corresponding to patients with neurocirculatory asthenia, and that in them, quantities of digitalis in excess of the calculated body-weight dose are required to slow the ventricles. In patients with auricular

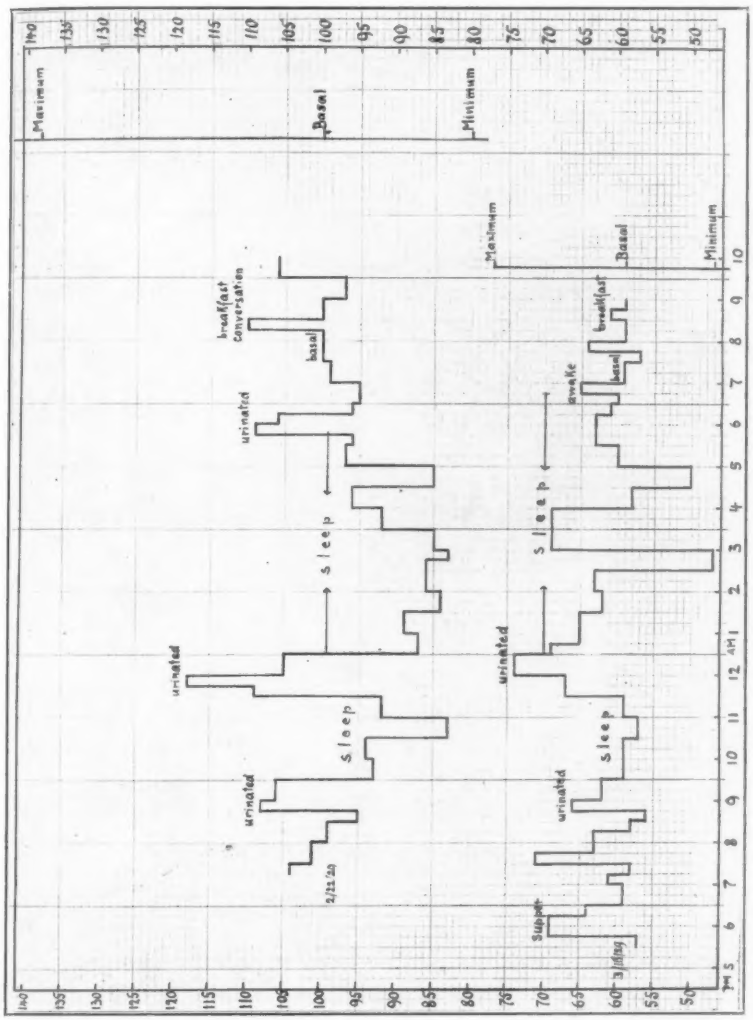

Fig. 1.—Heart rate in a phlegmatic individual with rheumatic mitral stenosis. Upper curve—undigitalized. Lower curve 36 c.c. tincture of digitalis in the preceding thirteen days.

fibrillation and a more stable ventricular rate the usual and smaller dosage with digitalis is efficacious in controlling the ventricular rate. It was pointed out that the dosage of digitalis necessary to achieve a certain effect depends as much on the vagus-accelerator balance as upon the body weight of the patient, and that patients with different nervous constitutions react differently to identical doses of digitalis when their auricles are fibrillating. Patients with increased acceler-

ator or sympathetic tone require large doses of digitalis to slow the ventricles, and tolerate these large doses without exhibiting toxic phenomena such as nausea or bigeminy.

It is my purpose, in this paper, to show that the relationship between vagus-accelerator balance and digitalis dosage may help to explain, not alone the varying tolerance to digitalis of individuals with differ-

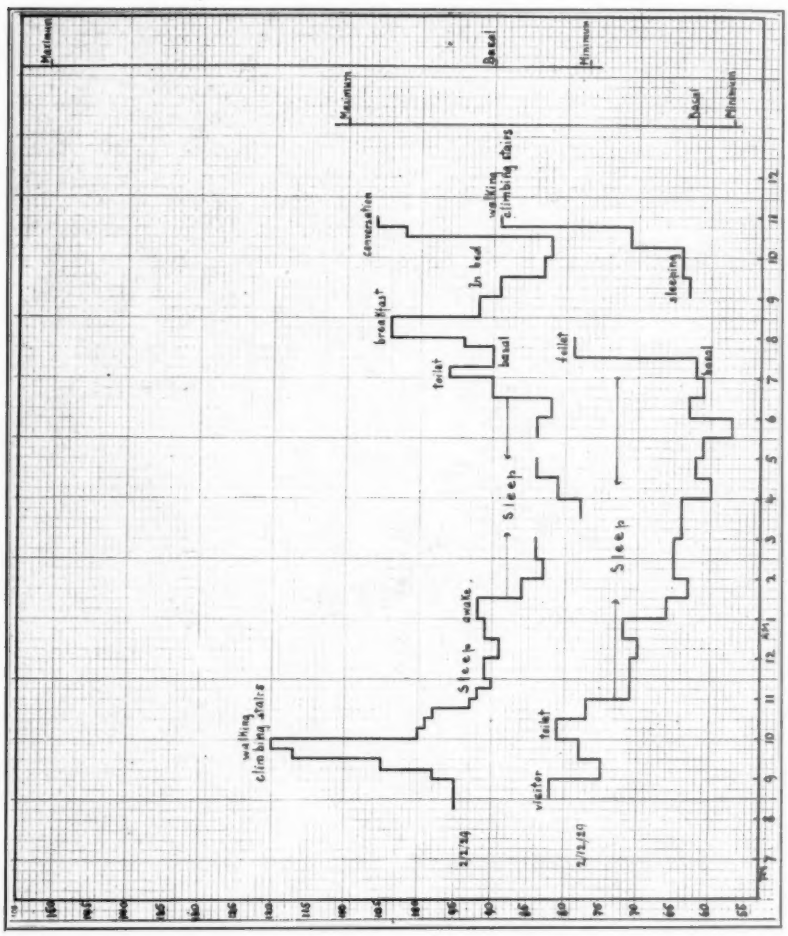

Fig. 2.—Heart rate in a woman with rheumatic mitral stenosis and neurocirculatory asthenia. Upper curve—51 c.c. tincture of digitalis from Jan. 21 to Feb. 2, 1929. Lower curve 44 c.c. tincture of digitalis from Feb. 3 to Feb. 12, 1929.

ently conditioned involuntary nervous systems, but also the variations in the effective therapeutic dose in auricular fibrillation at different ages, in fevers, in Graves' disease and in congestive heart failure.

Nervous Constitution.—The phlegmatic individual with rheumatic heart disease who develops auricular fibrillation is, as a rule, brought under the influence of digitalis with small doses. Fig. 1 is the chart of the ventricular rate of such a case: a woman aged thirty-three years, with rheumatic mitral stenosis, a heart showing great general enlargement, auricular fibrillation, but no congestive heart failure.

In addition she had a left hemiplegia of embolic origin of two years' duration. The upper record was taken at a time when she had received no digitalis for five months; the ventricular rate was not very rapid. The second tracing taken after 36 c.c. of the tincture of digitalis had been administered in the preceding thirteen days shows very adequate slowing of the ventricles.

In contrast to this case is the one represented in Fig. 2. This was a woman aged forty-six years who also had rheumatic mitral stenosis and insufficiency, and marked generalized cardiac enlargement, and auricular fibrillation. Her lungs were clear, and there was no edema, but the liver extended four fingers below the costal margin. During the first observation, although she had received 51 c.c. of the tincture of digitalis in the preceding twelve days, that is more than 4 c.c. a day, her ventricular rate was still labile and rapid. It was only after 44 c.c. more were given in the succeeding ten days that the ventricular rate was adequately slowed and stable. The patient was a very nervous excitable woman corresponding to the type exhibiting neurocirculatory asthenia.

Age.—Few accurate data are available regarding the influence of the age of the subject on the size of the effective dose of digitalis. McCulloch and Rupe,[3] studying children with normal hearts, found great variations in the dose necessary to produce a digitalis response. As criteria of digitalis action they used the appearance of sinus arrhythmia, slowing of the pulse, vomiting, or changes in the P-R interval and in the T-wave. They found that, as a rule, children required body-weight doses two to five times as great as those determined by Eggleston for adults. Jacobsen and Davison,[4] studying children with congestive heart failure, estimated the dosage for children as about twice that of adults. Schwartz and Weiss,[5] after administering a single full body-weight dose to each of 23 children, did not observe any toxic manifestations such as nausea or vomiting. In two children with auricular fibrillation adequate slowing of the ventricles resulted within twenty-four hours. Dr. May Wilson informs me that, in her experience, children require larger doses of digitalis relative to their body weights than do adults. On the other hand, Sutton and Wyckoff,[6] report that in children digitalis is effective in doses comparable to those required by adults, without necessarily producing intoxication.

In the elderly the pulse tends to be slow, and small doses of digitalis slow the ventricles in the presence of auricular fibrillation. Such a case is illustrated in Fig. 3, a record of the ventricular rate of a man of seventy years with auricular fibrillation who had a heart of normal size and shape, with no valvular disease, and a blood pressure of 120/65 mm. He exhibited a slow ventricular rate although he had received no digitalis. That this slow rate was not conditioned by an organic lesion of the conducting tissues is proved by the fact that

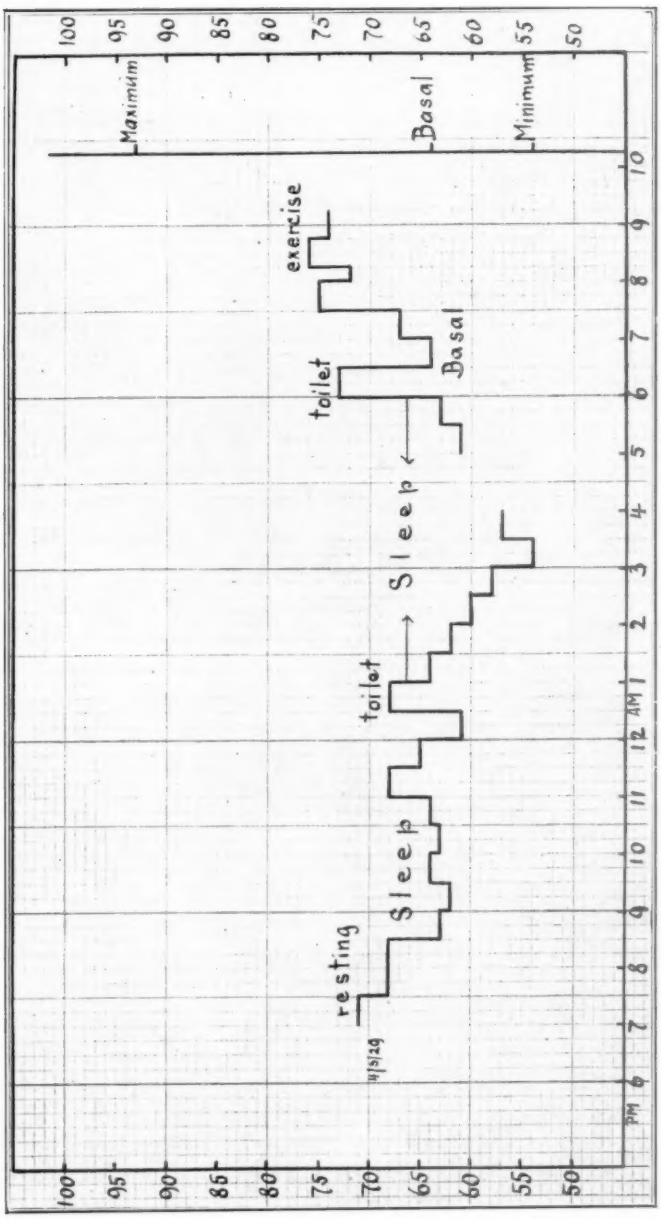

Fig. 3.—Heart rate in a man of seventy years, with arteriosclerosis. Undigitalized.

four weeks later he had normal sinus rhythm, and the electrocardiogram showed no delay in conduction.

On the other hand, it is well known that organic lesions of the conducting tissue, which occur particularly in older individuals, lead to slow ventricular rates in the presence of auricular fibrillation. Such a case is represented by R. L., a man aged sixty-seven years who had auricular fibrillation with a heart of normal size, without valvular lesions, and with a blood pressure of 140/70 mm. There was marked general arteriosclerosis. Under 3 c.c. of tincture of digitalis a day his heart rate ranged from 50 to 60. Sinus rhythm was restored with quinidine, and the heart rate remained unchanged. The P-R interval measured 0.25 seconds. Five days later auricular fibrillation again set in, and now free from the influence of digitalis the ventricular rate was 60 to 80.

Although exact experimental data are not available, it seems clear that, in general, in children, vagus activity is not marked, and sympathetic activity predominates; whereas with increasing age there is a shift in the balance of vagus and sympathetic to the side of increased vagus influence.[7] This phenomenon, in so far as it improves intracardiac conduction in children, and slows it in the elderly, helps explain the more labile ventricular rates in children and the more stable rates in the aged. It also makes understandable the fact that, as a rule, children must receive larger doses of digitalis than elderly individuals to control the ventricular rate when the auricles are fibrillating.

Fever.—The ineffectiveness of digitalis in slowing the pulse during fevers has long been noted, so that many clinicians do not use the drug when there is fever. Here we are concerned only with the effect of febrile states on hearts with auricular fibrillation, not with sinus rhythm. A diminished vagus, or increased accelerator activity, or both are operative in febrile states.[8, 9] Cohn and Jamieson,[10] found accelerated conduction from auricles to ventricles in 11 of 50 patients with lobar pneumonia. In the presence of auricular fibrillation this improved conduction leads to a rapid ventricular rate. Schwartz and Weiss,[5] were unable to slow the ventricles in children with active rheumatic fever and auricular fibrillation, with body-weight doses of digitalis, although in these same children the usual doses were effective when the infection had subsided.

In my experience patients with fever often tolerate much larger doses of digitalis than do normal individuals, and very large doses must be given to slow the ventricles when the auricles are fibrillating.[11] That such slowing can be achieved is illustrated by the following example:

A woman aged 45 years who had had mitral stenosis and auricular fibrillation for some time was admitted to Mt. Sinai Hospital with lobar pneumonia. When first seen she was intensely cyanotic and dyspneic, with a ventricular rate of about

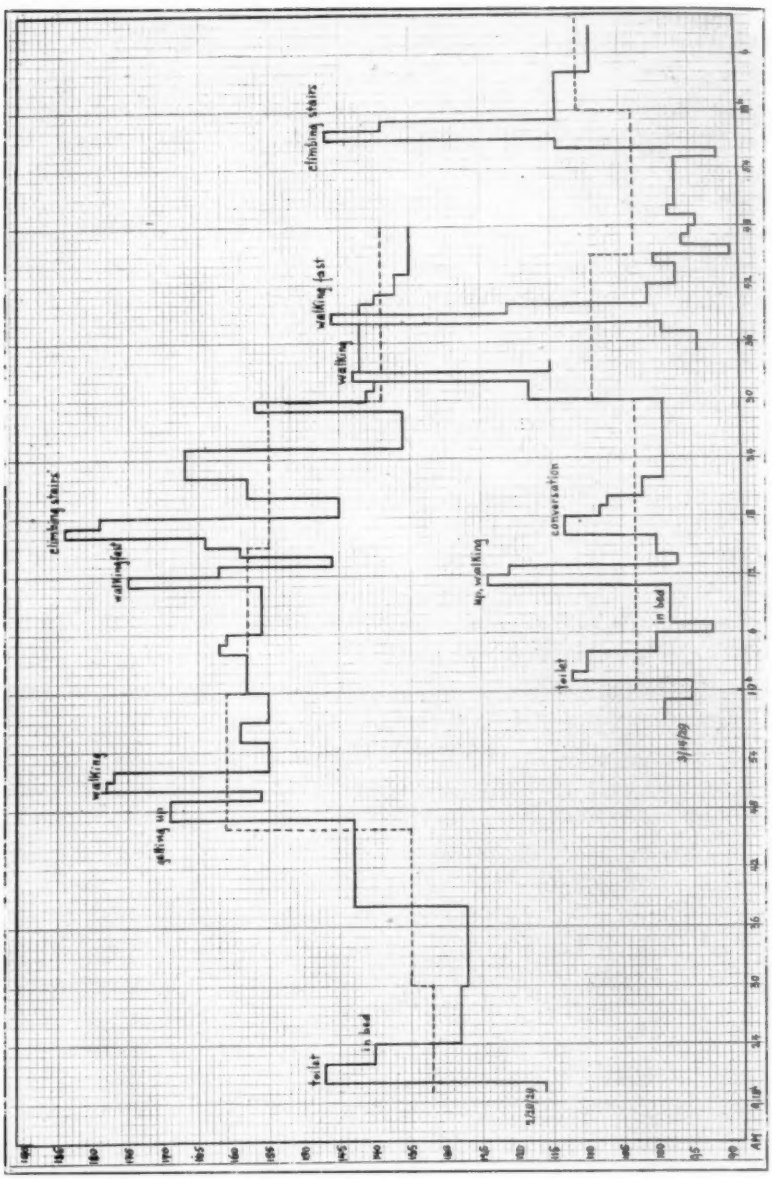

Fig. 4.—Unstable ventricular rate in a woman with Graves' disease. Upper curve—undigitalized. Lower curve after 61 c.c. tincture of digitalis in the preceding sixteen days.

150, respirations of 36, and temperature 103° F. She received 19 c.c. of the tincture of digitalis within the first twenty-four hours. Within fifteen hours her ventricular rate was 112, and at the end of twenty-four hours it was 97. She then received about 2 c.c. of the tincture daily, and during the following week while her temperature ranged from 101° to 102°, her ventricular rate remained between 60 and 70. With this there was very pronounced improvement in her condition.

This case shows that an adequate digitalis effect can be obtained in patients with auricular fibrillation and intercurrent febrile episodes, if sufficiently large doses are administered.

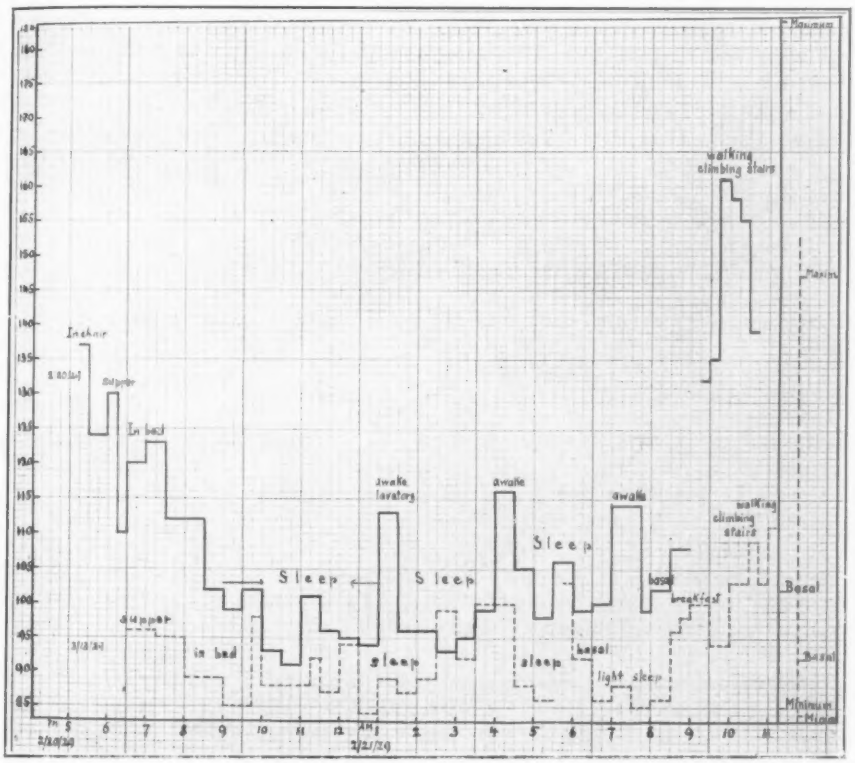

Fig. 5.—Heart rate in the same patient. Solid lines—undigitalized. Broken lines after 61 c.c. tincture of digitalis in the preceding sixteen days.

Graves' Disease.—In Graves' disease, as in fevers, the experience of clinicians has been that digitalis is ineffectual in slowing the heart rate, whether there be sinus rhythm or auricular fibrillation. Wenckebach states that patients with auricular fibrillation and Graves' disease do not react well to digitalis.[12] It has been my experience that patients with Graves' disease and auricular fibrillation, exhibit rapid ventricular rates, and that the ventricles react to all reflex stimuli by excessive acceleration. Very large doses of digitalis are required to slow the ventricular rate, and even after adequate slowing the ven-

tricles respond intemperately to reflex stimulation. These large doses can be tolerated without toxic symptoms. The following case offers a good illustration:

A woman aged 50 years was admitted to the Mt. Sinai Hospital Dispensary with classical signs and symptoms of Graves' disease. Two years previously, following an automobile accident, she had begun to lose weight and to tire easily, so that she was unable to do her housework. For six months she had had attacks of palpitation with a sense of suffocation. There was sweating, tremor of the hands and progressive loss in weight. Radium therapy had been ineffectual. On admission she exhibited slight exophthalmos, a von Graefe sign, a slightly enlarged thyroid isthmus, marked tremor of the hands. The heart showed considerable enlargement of the left ventricle, and auricular fibrillation. The basal metabolic rate was +65. Her heart rate was recorded by means of the cardiotachometer. Fig. 4 shows the ventricular rate recorded every few minutes both before and after digitalization. The excessive accelerations following moderate exertion are striking, even after she had received large doses of digitalis. In Fig. 5 is recorded the heart rate for two periods of about seventeen hours each, once before digitalis had been given, and after 61 c.c. of the drug had been given in sixteen days. There were no symptoms of digitalis intoxication, the rate during sleep did not go below 85, and a maximum of 147 was reached after exercise.

At times the increased tolerance to digitalis of a patient with Graves' disease may be of diagnostic value. This is well illustrated by the following case.

W. A., (hospital No. 325061) a man aged 60 years had had increasing weakness, dyspnea on exertion and palpitation for two years. For one month the symptoms had been worse. His weight one year ago was 195 pounds, his present weight 155 pounds. He was a serene, well built elderly man. The eyes were not prominent. The thyroid gland was not palpable, and there was no substernal struma visible on the roentgen film. The lungs were moderately emphysematous, with some râles at the right base. The heart was not enlarged, the sounds were rather faint, and there were no murmurs. The rhythm was absolutely irregular, with a ventricular rate of 150. The electrocardiogram showed auricular fibrillation. The blood pressure was 140/80 mm. There was considerable sclerosis of the radial and temporal arteries. The Wassermann reaction was negative. It was thought that the patient had auricular fibrillation associated with arteriosclerosis. There was no other evident etiological factor. Digitalis was administered. Twenty-one c.c. of the tincture were given in three days, yet the ventricular rate was 120. In the first nine days of treatment 46 c.c. of the tincture were administered; there was no nausea or bigeminy and the ventricular rate did not fall below 90. In the subsequent seven days 39 c.c. more of tincture of digitalis were given with no further drop in pulse rate. The unexplained resistance to the effects of digitalis led to the estimation of the patient's basal metabolism. This was found to be +54 on one occasion and +65 on another.

This case of atypical hyperthyroidism was discovered only because of the exceptionally high tolerance for digitalis.

When the Graves' disease is no longer active, this increased tolerance for digitalis is lost. Thus Fig. 6 represents the ventricular rate a woman of fifty years who had developed Graves' disease six years

previously. Four years previously she had an enlarged heart with auricular fibrillation, and cardiac failure. The activity of the Graves' disease gradually receded and the cardiac signs and symptoms domi-

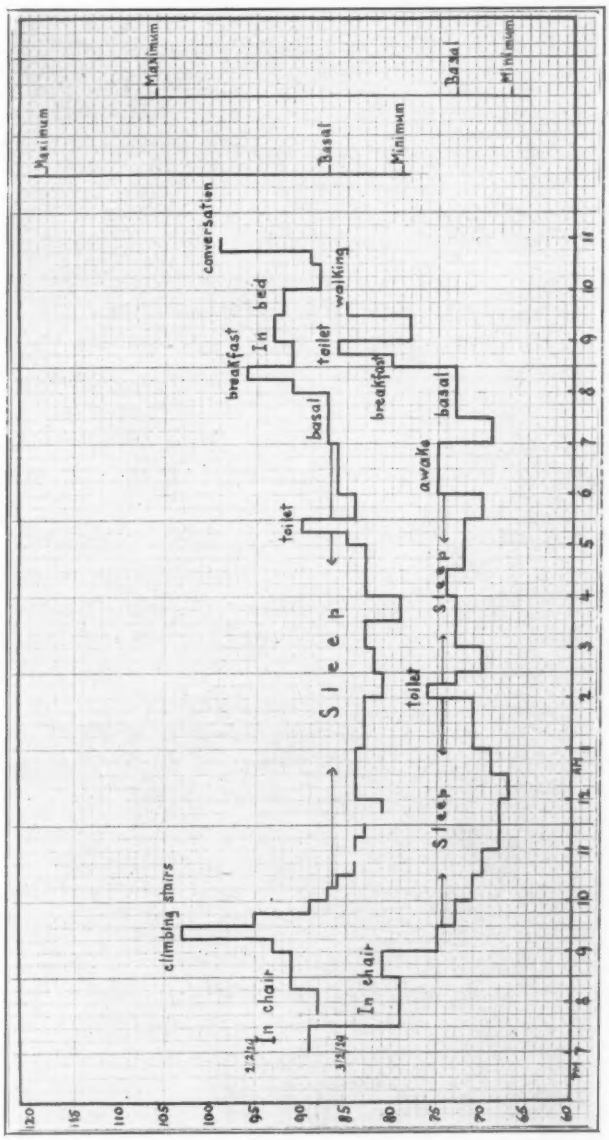

Fig. 6.—Heart rate in a woman with inactive Graves' disease. Upper curve after 17 c.c. tincture of digitalis from Jan. 19 to Feb. 2, 1929. Lower curve, after 23 c.c. tincture of digitalis from Feb. 13 to March 2, 1929.

nated the clinical picture. When the present record was taken the Graves' disease was inactive, the heart showed enlargement of all chambers, and the liver extended four fingers below the costal margin. Daily doses of from 1 to 2 c.c. of the tincture of digitalis adequately controlled the ventricular rate.

Cardiac Insufficiency.—Acceleration of the heart rate with the onset of cardiac insufficiency, in the presence of normal sinus rhythm, is a commonplace clinical observation. The physiological processes that underlie this quickening of the heart are complex and are not fully understood. Alterations of certain chemical factors, such as the hydrogen-ion concentration, the carbon dioxide and oxygen content of the blood, and the accumulation of lactic acid may play a rôle. Another important mechanism is often overlooked. Bainbridge[13] showed that a rise of venous pressure, or a sufficient increase of the diastolic distension of the heart, brings about reflex acceleration of the heart, due partly to loss of vagal tone, and partly to an increase of accelerator tone. Such reflexes must often be active in the presence of myocardial insufficiency. Kisch[14] has stressed the diminution of vagus tone and the increase in sympathetic tone in circulatory failure, and has ascribed the increased heart rate to this factor. In addition to the Bainbridge reflex, reflexes arising in the carotid sinus undoubtedly play a rôle.

The same mechanism must prevail in heart failure associated with auricular fibrillation, but here the preponderance of sympathetic activity leads to increased conduction from auricles to ventricles, and so to an increased ventricular rate. So it is that, in the presence of marked cardiac insufficiency, larger doses of digitalis are required to slow the ventricles than when compensation has been restored. Mackenzie,[15] long since, noted this phenomenon, and ascribed it to a diminished irritability of the A-V node as the clinical condition of the patient improved. More recently Gold and DeGraff[16] presented data to show that "the degree of heart failure is an important factor in determining the amounts of digitalis necessary to produce full therapeutic results." Their patients with severe heart failure required much larger doses to slow the ventricles than did these who were ambulant.

Some authors believe that patients with auricular fibrillation differ in their sensitivity to digitalis because of differences in the nature and cause of the underlying heart disease. Thus, the slow ventricular rates observed in elderly patients with auricular fibrillation are ascribed to sclerotic lesions of the conducting system. I have compared cases of auricular fibrillation associated with rheumatic heart disease, hypertension, arteriosclerosis, and Graves' disease, and have found that the etiological agent or the anatomical lesion rarely is the determining influence. Differences in tolerance, when they exist, are best explained by the varying state of vagus-accelerator balance. In Graves' disease it is the increased sympathetic activity, in the elderly with arteriosclerosis, it is, as a rule, the increased vagus influence, so common in the aged, rather than fibrotic lesions of the conducting system that governs the reaction of the heart to digitalis.

DISCUSSION

The data that have been presented seem to allow of the following generalizations. In the absence of organic lesions of the conducting system, the ventricular rate in patients with auricular fibrillation is determined by the vagus-accelerator balance, fast and labile rates being associated with preponderant sympathetic action. In patients in whom sympathetic activity is dominant, larger doses of digitalis are required to slow the ventricles, and these larger doses are tolerated without giving rise to toxic symptoms. In childhood, as well as in patients with neurocirculatory asthenia, fever, Graves' disease, and with severe circulatory failure the activity of the accelerator nerves outweighs that of the vagus, and it is just in these clinical conditions that the largest doses of digitalis must be administered to bring about ventricular slowing.

Certain analogies between the slowing of the heart in response to vagus pressure and to digitalis were pointed out some fifteen years ago by Weil[17] and by Fahrenkamp.[18] The latter showed that in patients with auricular fibrillation and rapid ventricular rates vagus pressure induced no ventricular slowing, and that large doses of digitalis were also without effect; that in those patients in whom ventricular slowing followed doses of 1 to 2 grams of digitalis there was definite slowing following vagus pressure; and that patients who exhibited a marked vagus effect were sensitive to small doses of the drug. These observations have led to the generalization that the effectiveness of digitalis medication in patients with auricular fibrillation in general will parallel the degree of ventricular slowing they exhibit following pressure on the carotid sinus.[19]

These phenomena reveal the same mechanism that we have described. Presumably, vagus slowing of the heart is induced with greater difficulty when the sympathetic is overactive, and this is true whether the slowing is brought about by mechanical pressure or by digitalis. The regulation of the heart rate is so complex, and there are so many variables involved, that one cannot expect to find, in every individual case of auricular fibrillation, an exact quantitative relationship between vagus-accelerator balance, ventricular rate, and digitalis susceptibility. Yet there is no doubt that this mechanism is, to a large extent, determining. It is very probable that the variable response to digitalis of hearts with normal sinus rhythm is controlled by the same factors. Cohn[20] has shown that with sinus rhythm, in the absence of edema, digitalis reduces the rate principally in hypodynamic unstable hearts.

In the treatment of patients with auricular fibrillation, the lability of the ventricular rate is as significant as its absolute level. The marked lability of the heart rate in many patients with auricular fib-

rillation, even when they are under the influence of digitalis, has been pointed out in a previous communication,[2] and is well illustrated in some of the graphs of the present paper. This variability is evidenced to a much greater degree by individuals with preponderant sympathetic activity. In them, more especially, quantities of digitalis sufficient to produce satisfactory ventricular slowing when they are at rest, are quite inadequate when they are up and about. Very large doses of the drug may be necessary to keep the ventricular rate within

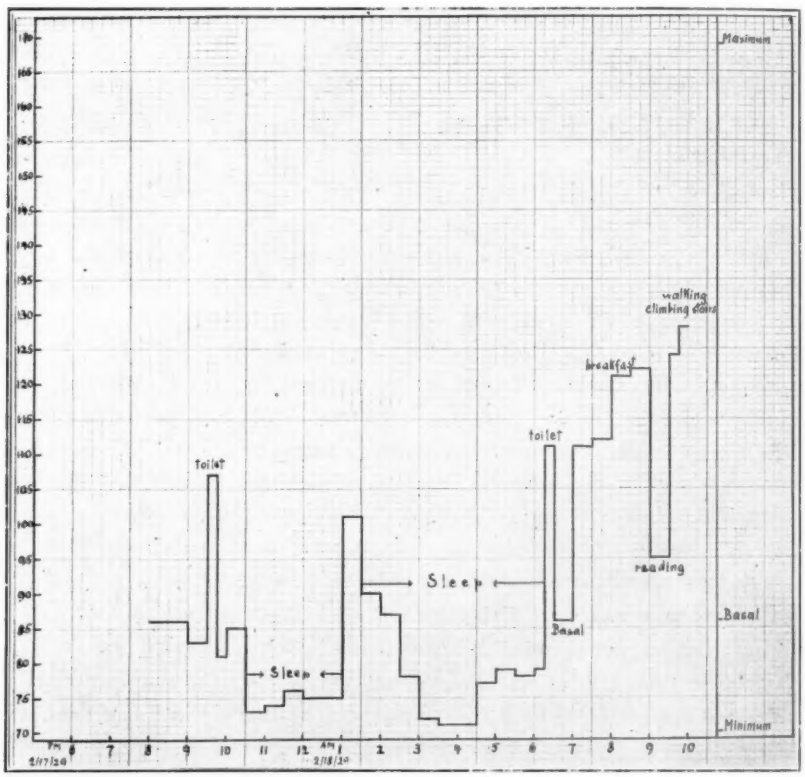

Fig. 7.—Response of ventricular rate in auricular fibrillation to slight exertion.

bounds under such conditions. Fig. 7, representing the ventricular rate of a man with mitral stenosis and auricular fibrillation, shows that although at rest the rate ranges from 75 to 85 a minute, slight exertion, such as eating breakfast, elevates it to 125. To such patients enough digitalis must be given to reduce the ventricular rate at rest to from 50 to 60 a minute, to prevent undue acceleration when they resume their ordinary activities. At times it is impossible to check these unregulated responses of ventricular rate to physical or even emotional activity. For two years I have had under observation a

man with chronic rheumatic valvular disease, mitral stenosis and auricular fibrillation, and a marked anxiety neurosis. He has never had congestive heart failure. The following observations are typical of his reactions to digitalis. Undigitalized, his ventricular rate was about 150. After he had received 52 c.c. of the tincture in ten days the ventricular rate when he was in bed before breakfast was 56. After breakfast it rose to 112; while he was being examined to 120; and after walking across the room to 160. In the following seven days 44 c.c. more of the tincture were given. At the end of this time the rate was 58 at rest, and 80 walking. Because of the development of toxic symptoms, such as headache and anorexia, it has been impossible to keep him adequately digitalized, and he has had repeated courses of quinidine to maintain sinus rhythm, as the only means of keeping him comfortable. It is necessary constantly to reiterate that in the treatment of auricular fibrillation enough digitalis must be given to maintain ventricular slowing when the patient is pursuing his ordinary activities; and that for patients with increased accelerator tone this involves doses much larger than those required to slow the ventricles with the patient at rest.

What practical rules of digitalis dosage may be derived from all of these considerations? The weight of the patient is no absolute guide to the total dose of digitalis that is required. Of equal, if not greater importance is the vagus-accelerator balance. Preponderant accelerator activity manifests itself clinically by a rapid labile ventricular rate, and by many of the signs and symptoms of neurocirculatory asthenia. It is particularly marked in patients with Graves' disease, neurocirculatory asthenia, and severe cardiac insufficiency. It may be anticipated that such patients will require exceptionally large doses of the drug to slow the ventricles in the presence of auricular fibrillation.

In actual practice, when dealing with a patient who has received no digitalis, it is convenient to use the calculated body-weight dose as a rough preliminary guide. One can commence by giving as the first dose, one-half of the theoretical dose which is approximately 0.18 c.c. of the tincture per pound. At the end of six hours 4 c.c. of the tincture are given, and this dose is repeated once after six more hours. Then 2 c.c. are given every six hours until the ventricular rate at rest is about 60. In patients who do not exhibit hyperactivity of the accelerator nerves such dosage very quickly will bring about satisfactory slowing of the ventricles. In those with heightened sympathetic activity this relatively high dosage may have to be continued for many days before the ventricles are controlled. It may be given without fear of toxic manifestations, for these patients rarely show evidences of toxicity before a well-marked slowing of the ventricles occurs. Of

course the patient must be under continuous observation to guard against possible overdosage as manifested by nausea, vomiting, or bigeminy.

Patients with cardiac failure often vomit shortly after taking the drug. This is not a specific digitalis effect, but is probably related to congestion and irritability of the stomach, and is not an indication for suspending further digitalis therapy. In such cases the substitution of the dried leaf for the tincture often enables the patient to retain the drug.

The size of the maintenance dose, once the patient has been digitalized, cannot be predicted, but must be established by actual trial in each case. In general, the greater the original dose that was required to slow the ventricles, the larger will be the maintenance dose. It may range from 1 to 4 or 5 c.c. of the tincture a day. It must serve to control the ventricles when the patient is following his usual mode of life.

All such rules, at best, are but rough guides. Strict individualization and giving enough of the drug to produce the desired effect, irrespective of the size of the dose, are the essence of successful therapy.

SUMMARY

The ventricular rate in patients with auricular fibrillation is largely governed by the balanced activity of the vagus and accelerator nerves. With preponderant vagus activity the rate tends to be slow and stable, with preponderant accelerator activity it tends to be rapid and labile. Patients in whom accelerator influences predominate require much larger doses of digitalis to slow and stabilize the ventricular rate than do those in whom this excess of sympathetic influence is not manifest. This factor of nervous regulation is more potent than the weight of the patient in determining digitalis dosage. The conditions under which auricular fibrillation associated with exaggerated accelerator activity is encountered most frequently in the clinic are: in childhood, in patients with neurocirculatory asthenia, with fever, with Graves' disease, and with severe cardiac insufficiency. In these conditions exceptionally large doses of digitalis must be given to produce and maintain adequate ventricular slowing in the presence of auricular fibrillation.

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THE EFFECT OF DIGITALIS ON THE T-WAVE OF THE ELECTROCARDIOGRAM. AN EXPERIMENTAL STUDY IN HUMAN BEINGS*

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FLATTENING or inversion of the T-wave in the electrocardiogram following administration of digitalis has been reported by a number of observers, many of whom regard this change as an early sign of digitalis effect or intoxication (Pardee;[8, 9] Cohn, Fraser and Jamieson;[3] Marvin, Pastor and Carmichael;[5] Cohn and Stewart[4]). Robinson and Wilson[10] considered such a change in the T-wave as the first evidence of digitalis intoxication. Others found that the T-wave remained upright and became taller after digitalis (Yacoël and Papanaÿotou;[12] Selenin;[11] Nicolai and Simons[7]). There is a general impression in spite of these contradictory reports that inversion or flattening of the T-wave is reliable, early evidence of digitalis effect. McCulloch and Rupe[6] found inversion of the T-wave in only 11 per cent of children following digitalis administration while about 33 per cent showed changes in rate and conduction.

In a previous publication one of us (W.A.B.[2]) reported a series of experiments on dogs in which different preparations of digitalis were administered by various routes and in ascending doses until death of the animal occurred. Electrocardiograms were taken three times each day for the duration of the experiment. In not a single instance did the T-wave become inverted in spite of the fact that evidences of digitalis intoxication were present, such as prolonged P-R interval, nodal rhythm, complete dissociation, nausea and vomiting. These results have since been confirmed by Blumenfeldt and Strauss[1] who used rabbits and human patients with cardiac disease, including auricular fibrillation.

It seemed desirable to perform experiments on human beings who had neither a history nor evidence of cardiac disease, since it is possible that persons with healthy hearts react differently from those with cardiac disease. These experiments were conducted like those of the animal series, namely, gradually ascending doses of digitalis were given and electrocardiograms were taken three times each day in order not to overlook early or transient changes—a precaution not taken by some observers who failed to note an inversion of the T-wave.

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Nine adult, volunteer patients were selected who were convalescing from peptic ulcer, arthritis and like conditions but who gave no history or evidence of cardiac disease. Digifoline was given once a day intravenously, beginning with 1.0 c.c. and increasing by 1.0 or 2.0 c.c. daily until these ascending doses produced nausea, vomiting and precordial distress. The usual amounts given were 45.0 c.c. in nine days, the patient receiving 24.0 c.c. during the last three days of the experiment. The drug was standardized shortly before use, and it was found that 1.0 c.c. was equal to 1.5 grains of the powdered leaf. Control electrocardiograms were taken before the drug was given and at three, seven and twenty-four hours after each dose. The usual precautions were observed while the electrocardiograms were taken.

Analysis of the electrocardiograms so obtained failed to reveal a single instance of inversion of the T-wave. Nor was there any instance of a previously upright T-wave becoming isoelectric. This was not due to lack of potency or to insufficient dosage of the drug as eight of the nine patients showed a moderate drop in pulse rate, one eventually developed partial heart-block (P-R interval of 0.34 second) and another developed 2:1 heart-block and later, transient auricular fibrillation. All became nauseated and vomited; most complained of a distressing form of precordial oppression.

A slight reduction in amplitude of the T-wave occurred in five cases, the decrease being from 1 to 3 mm. Similar reductions and increases were occasionally seen without other signs of intoxication. There were times when the T-wave decreased slightly after digitalis but would return to the previous level after the next dose which would be larger. In the two patients in whom block developed the T-wave actually increased slightly in amplitude at the time block appeared.

It seems that variations of from 1 to 3 mm. in amplitude of the T-wave should be considered as possibly due to extracardiac causes. The changes in amplitude of T were compared with the corresponding changes in QRS. The two were seldom simultaneously depressed to a proportionate degree. In fact, changes in the opposite direction occurred at times.

The results of our experiments, both on human beings and on animals, lead us to the conclusion that inversion of the T-wave does not always occur, even after toxic doses of digitalis, nor is it always an early sign when it does occur. We cannot regard T-wave inversion as a reliable or early sign of digitalis action. The slight changes in T-wave amplitude might be due to extracardiac factors and position changes of the heart. This should be ruled out before ascribing such changes to digitalis.

SUMMARY

A series of experiments was conducted on persons without history or evidence of heart disease in order to determine the effects of digi-

talis on the T-wave of the electrocardiogram. Ascending doses were given intravenously, daily, until nausea, vomiting, precordial distress and heart-block developed as signs of digitalis excess. In no instance was there an inversion of the T-wave. Minor decrease in the amplitude of T occurred in about one half of the patients but the degree of reduction can be explained on other grounds and an elevation of the same extent occurred at times, viz., when heart-block occurred. Inversion of the T-wave cannot be regarded as an early or constant sign of digitalis effect. This was shown in these experiments in persons without heart disease and in dogs, and similar results have been reported in patients with cardiac disease.

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A NEW METHOD FOR CLINICAL DETERMINATION OF HUMAN CAPILLARY TENSION*

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INTRODUCTION

A STUDY of the various methods for measuring capillary blood pressure in man reveals that most of them are inadequate for routine clinical investigation for one or both of two reasons: (1) They are not practicable in regard to clinical application. (2) The results obtained are not accurate. To be available clinically, a method must have neither of the above faults. We have devised a new instrument and a new technic which, we believe, fulfill both requirements.

REVIEW OF PREVIOUS METHODS

Roy and Brown[1] (1875), although not studying human capillaries, deserve mention as the first to conceive a practical apparatus for the indirect measurement of the tension in capillaries as viewed with a microscope. With an air-filled capsule covered by a transparent animal membrane, pressure was applied to the capillaries in the web of a frog, as seen under the microscope. The principle of this method was used in modified form in the tonometers of many later investigators for application to man.

Methods for measuring human capillary pressure fall into two distinct categories: (1) those measuring so-called arteriocapillary pressure; (2) those attempting to measure actual capillary pressure.

In the first group, three methods are worthy of mention. Mosso[2] (1895) used a metallic glove filled with warm water over the middle and ring fingers. Pressure was applied through the medium of the water, and oscillations were transmitted to a kymograph. Oscillations of maximum amplitude were taken as the criterion of mean tension. Gaertner[3] (1899) compressed the second phalanx of the finger by means of a pneumatic ring. On decompression, the instant of reappearance of redness was taken as the end-point for determination of capillary pressure. Kreidl[4] (1902) employed, at the base of the nail, a half-ring attached to a lever, which oscillated on a drum, to obtain the so-called arteriocapillary pressure.

The readings obtained by these men were certainly not measurements of capillary pressure. Capillaries do not show the oscillation

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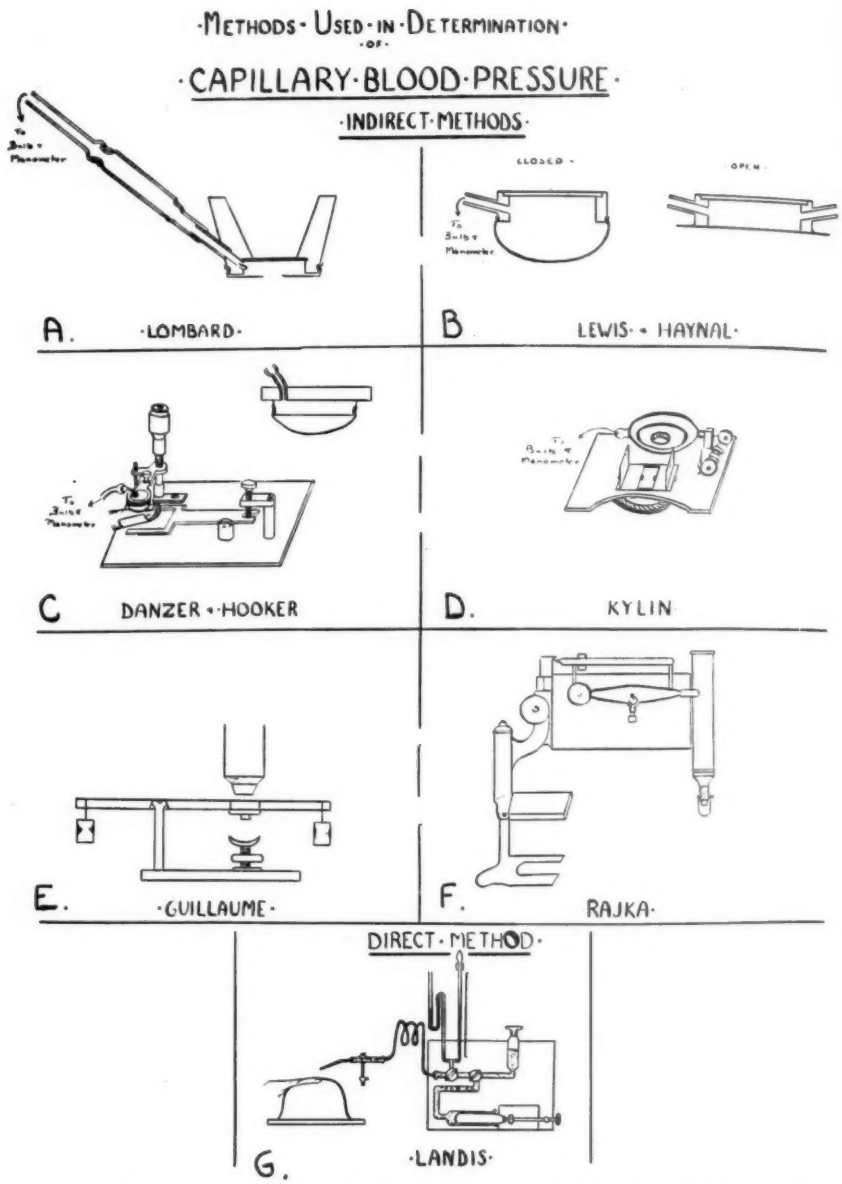

Fig. 1.—Previous methods used in determination of capillary blood pressure in man.

phenomena on which these methods were based. The actual figures obtained were about three times higher than those of capillary pressure as determined by later workers.

In the second group are those methods which purported to measure actual capillary pressure. These fall into two classes: (1) direct, (2) indirect.

The direct measurement of capillary pressure in man by actual intubation under control of a microscope was first undertaken by Carrier and Rehberg[5] (1922).

Landis[6] (1930) (*see* Fig. 1 *G*) devised a much more accurate method for micro-injection of the human capillary. A micropipette with an orifice of 8-12 micra in diameter is used. It is controlled by a Chambers[7] micromanipulator which is capable of moving it in three planes. The pipette is filled with fluid from a reservoir and connected to a manometer. Pressure is applied until only a few corpuscles remain oscillating at the tip of the pipette. A reading is then taken.

This method is probably the most accurate of all to date. Unfortunately, it is not adaptable to clinical use. It requires an extremely high degree of skill on the part of the operator, and an even higher degree of patience on the part of the subject. Special training is necessary to operate the micromanipulator successfully. To apply it to micro-injection of human capillaries is a task for the expert. Then, too, before insertion of the pipette into a capillary, it is always necessary to remove a thin layer of epidermis with a keen razor blade. Even with this precaution, the author states, breakage occurs frequently. Landis' apparatus, however, obviates many technical errors of the method of Carrier and Rehberg, so that the results obtained may be taken as the standard measurement of capillary pressure in the human. It follows, then, that only those instruments which give results comparable to those of Landis are sufficiently accurate.

Another form of the direct method of measuring capillary pressure is that of Basler[8] (1914) and Weiss[9] (1914). These men pricked the finger and applied to the bleeding point a tube filled with warm salted serum plus hirudin. In the tube was a piston which could slide up and down easily. By maneuvering the piston, the pressure necessary just to stop bleeding could be determined. The criticism of this method is obvious. The equilibrated pressure cannot be proved to be capillary. The bleeding probably comes from arterioles, capillaries, and venules of varying caliber. Problems in technic, such as proper sealing of the tube to the skin and prevention of clotting, add to the difficulties in using this method clinically.

Indirect methods for measuring capillary pressure fall into two groups: (1) those using blanching of the skin as an end-point; (2) those using as the end-point some phase of cessation of flow, as visualized microscopically.

Von Kries[10] (1878) was the first to propose the use of color modifications in the skin to measure capillary pressure. He devised a simple movable stand which was applied to the skin at a definite area. Weights were added until blanching occurred. The method was later modified by von Basch[11] (1900) and by von Recklinghausen[12] (1906), who used glass capsules sealed to the skin and filled with air at measurable pressures. Basler[13] (1912) devised an elastic closed capsule to apply pressure. The latter is interesting as the forerunner of later methods using elastic compression. More recently, Marks[14] (1920) described a similar capsule. He asserted that compression with blanching as the end-point was the only clinical method then available for measuring capillary pressure. Ariola[15] (1925) devised a similar instrument.

The results obtained by these methods cannot be accepted as accurate measurements of capillary pressure because: (1) It has been shown repeatedly by various workers (Danzer and Hooker[16]; Boas[17]; M. Weiss[18]) that initial blanching of the skin is due chiefly to an evacuation of the superficial venous plexuses. Skin blanching occurs before flow in the capillaries, as visualized microscopically, is affected. (2) Blanching of the skin does not offer a reliable end-point. The skin of different subjects shows a great variation in the amount of pigment it contains. Then, too, there is the great personal factor as to what constitutes initial blanching. The strongest evidence of the fallacy of the method is that different workers with the same device have obtained quite varying results (Friedenthal[19]).

Hill[20] (1920) applied pressure by focussing a fine jet of water on the skin at the nail-bed. The jet was slowly moved to and fro and the pressure slowly increased. Initial paling of the skin was taken as the end-point for capillary pressure determination. The hand was then raised to empty the veins, while a cuff on the arm compressed the arterial flow. The jet of water was again used to cause paling of the skin. The second reading was subtracted from the first to give the final result. As noted above, the results of Hill probably represent the pressure in the small venous plexuses of the skin rather then that in the capillaries or arterioles. Again, the difficulty of knowing what constitutes initial paling of the skin presents itself.

Lewis and Haynal[21] (1928) (*see* Fig. 1 *B*), working on histamine flares in the human skin devised a method for measuring what they termed venule pressure. Histamine, when injected into the human skin, causes a local dilatation of the small arterioles, and, as these authors asserted, a passive dilatation of the capillaries. Three to twelve minutes after injection of histamine, pressure was applied to the reddened area through either an open capsule sealed to the skin or a closed capsule until blanching back to normal was secured. The readings obtained were taken to represent close approximations to capillary pressure.

The physiological basis of this method is disputed by Krogh and Rehberg,[22] who maintain, on the basis of their work, that the capillary dilatation with histamine is an active one. Also, and what is more important, different workers with the device obtain widely varying results. Thus, Weiss and Ellis[23] (1929), using the same method, get measurements about one-fifth those of Lewis and Haynal. At any rate, it is difficult to see how a method which produces abnormal changes in the smaller vessels of the skin could be used to measure accurately the normal pressure in these vessels.

Most of the modern methods for measuring capillary pressure utilize visualization of the capillaries in the nail-bed as a basis.

Heuter[24] (1879) was the first to observe living capillaries in the human. Lombard[25] (1911) was the first to put this observation into practice by utilizing it in measuring capillary pressure. He placed a drop of glycerine at the base of the nail, focussed on the area with a microscope with a magnification of 65x, and saw entire capillary loops with the streaming of corpuscles in them. Anatomically, the capillaries in the skin papillae are arranged vertically everywhere except at the base of the nail, where they lie more or less horizontally. For this reason, only the top of the capillary loop can be seen in other parts, while at the base of the nail the entire loop can be examined (Spalteholtz[26]; Callander[27]).

Lombard (*see* Fig. 1 *A*) applied pressure to the skin by means of an open capsule filled with glycerine. Glycerine is a very poor medium for conducting pressure. Because of its high viscosity, pressure changes are transmitted only slowly. Krauss[28] (1914) used a chamber covered at one end by goldbeater's skin. Pressure was applied by means of a bulb connected to a manometer which measured the tension. A magnification of 10x was used. Although Krauss claimed to see the cutaneous vessels, his index was probably skin blanching. Danzer and Hooker[16] (1920) (*see* Fig. 1 *C*) devised a method based on the principles of the Krauss instrument. They employed a capsule which was less cumbersome, but which was also covered by goldbeater's skin. A microscope was used to determine their end-point. Kylin[29] (1921) (*see* Fig. 1 *D*) also constructed an instrument on similar principles, differing only in size and form of construction. The results obtained by these methods correspond closely, and are probably as accurate as can be obtained by the indirect method. Clinically, however, these instruments present two important practical difficulties. Goldbeater's skin, made from the outer coat of the cecum of an ox, is not readily procurable in this country. The technic of making it transparent is difficult and, even in experienced hands, about 80 per cent of the prepared membranes are unfit for use. When employed with best precautions, the skin collects dust and clouds comparatively quickly. Since it cannot be cleaned satisfactorily, it is then of little value. Furthermore,

these methods require the services of two men, one to watch the capillaries, the other to apply and record the pressure. Thus, we found these methods not to be as clinically practicable as their author claimed.

The use of an elastic membrane for transmitting pressure has been attacked more recently. It has been maintained by Guillaume[30] (1924) and Rajka[31] (1926) that all the pressure produced is not transmitted to the capillary because of the loss on the sides of the finger due to elasticity of the membrane. These workers also have asserted that to be available as a clinical method any device for measuring capillary pressure should be operable by one man. Guillaume (*see* Fig. 1 *E*) constructed a simple lever from which projected a small piece of glass of known area which made contact with the finger. At the end of the lever was a cup into which weights could be dropped to apply pressure. Unfortunately, there was no simple means of grading the pressure applied. To get accurate results would necessitate considerable manipulation of weights with attendant consumption of time. Rajka (*see* Fig. 1 *F*) devised a complicated device for applying pressure through a rigid surface. The great amount of inertia in the system probably explains his low readings. It is obvious that capillary pressure must be higher than venous pressure. The figures obtained by this investigator are lower than the accepted values for venous pressure. Besides, this method requires too complicated a device for practical work.

Measurements of normal human capillary pressure as obtained by these various methods are:

I. Measurement of arteriocapillary pressure:		
a. Mosso[2]	1895	60-70 mm. Hg.
b. Gaertner[3]	1899	60-80
c. Kreidl[4]	1902	55-65
II. Measurement of actual capillary pressure:		
A. Direct methods:		
1. Intubation methods:		
a. Carrier and Rehberg[5]	1922	4.5-7.5
b. Landis[6]	1930	12-32
2. Bleeding methods:		
a. Basler[8]	1914	7.7-13
b. Weiss[9]	1914	10
B. Indirect methods:		
1. With skin blanching:		
a. Using normal skin coloration:		
(1) von Kries[10]	1878	24-38
Natanson[32] (von Kries method)	1886	71
(2) von Basch[11]	1900	25-30
(3) von Recklinghausen[12]	1906	55
Krogh and Rehberg[22] (von Recklinghausen method)	1928	5- 8
(4) Basler[13]	1912	7- 9
Landerer[33] (Basler method)	1913	17-25
Goldman[34] (Basler method)	1914	5- 7
(5) Marks[14]	1920	6-20
(6) Hill[20]	1920	10
(7) Ariola[15]	1925	10-14

b. Using histamine flares:		
(1) Lewis and Haynal[21]	1928	50-60
(2) Weiss and Ellis[23]	1929	6-12
2. With direct visualization of capillaries:		
a. Pressure applied by rigid surface:		
(1) Lombard[25]	1911	30-45
(2) Guillaume[30]	1924	18-28
(3) Rajka[31]	1926	1- 2
b. Pressure applied by elastic capsule:		
(1) Krauss[28]	1914	10
(2) Danzer and Hooker[16]	1920	20-24
Boas[35] (Danzer and Hooker method)	1922	20-30
(3) Kylin[29]	1921	13.6
Rominger[36] (Kylin method)	1923	8
Liebesny[37] (Kylin method)	1923	32.5
Nevermann[38] (Kylin method)	1924	6-11
Grzechouriak[39] (Kylin method)	1924	6-14

A glance at the foregoing table reveals the markedly varying results which investigators using the same or similar methods have obtained. The discrepancies are probably best accounted for by: (1) differences in the criteria of the end-point of a determination; (2) marked differences in the time required to take a reading—a fact which has an important bearing on the accuracy of the results, as will be indicated presently.

It would appear, therefore, that an indirect method which permits of a definite end-point and which also enables even an unskilled operator to take a reading in a very short time, would be the method of choice for routine clinical application—provided that it were shown to be sufficiently accurate. We have devised a new method for the clinical determination of human capillary pressure which, in our opinion, meets these requirements.

APPARATUS AND METHOD

Essentially the apparatus consists of a lever (Fig. 2 *D* [a]), a spring (d), a finger rest (e), and a scale (c). The lever is approximately 20 cm. long. At one end it contains a circular plate of glass (b) to which is attached a smaller plate of glass (f), 2 mm. in diameter. Between the glass and the fulcrum, a screw is inserted into the lever which has attached to it a spring (d), the other end of which is attached to the base of the instrument. On the lever rests a movable rider (g), used in calibration of the instrument. The pointer of the lever is in propinquity to a scale. A rest (e) is provided for the finger, which can be raised or lowered at ease in a vertical plane to bring the latter into proper relationship to the glass (f). The lever can be kept level by adjustment of the screw which regulates the tension of the spring.

The instrument can be placed conveniently on the stage of a microscope and clamped there to prevent movement. Reflected light is used. The stronger the light concentrated at the point of examination, the clearer the view of the capillaries obtained. Good results, how-

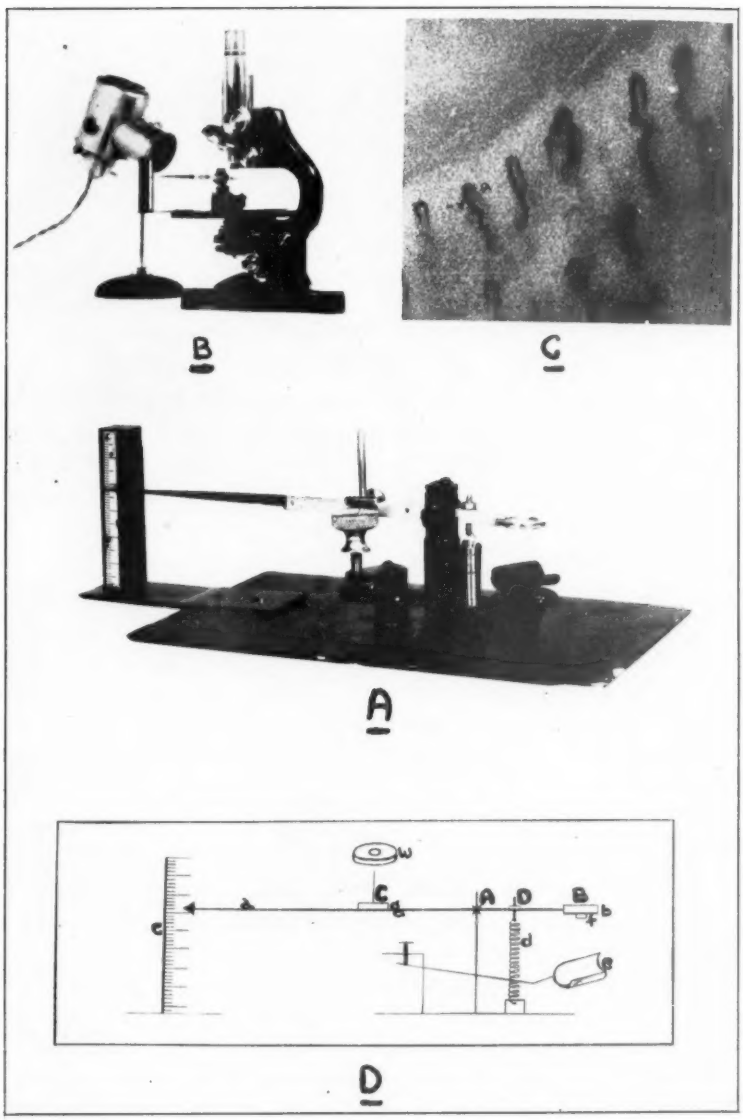

Fig. 2.—*A*. Photograph of the authors' clinical tonometer for measuring human capillary blood pressure. *B*. The instrument on a microscope stage ready for use. *C*. Photograph of the capillaries at the nail-bed, showing (a) arterial loop and (v) venous loop. *D*. Sketch showing the principles of construction of the instrument.

ever, can be obtained by placing an ordinary microscope lamp on the base of the instrument, which is on the stage of the microscope, so that the light is concentrated on the finger. A magnification of about 90-100x is used.

Calibration of the instrument is simple. A known weight (w) is placed on the rider which is on the lever. Then we know that:

$$1.\ AD \cdot X_1 = AC \cdot w$$
$$\text{and } 2.\ AD \cdot X_2 = AB \cdot P$$
$$\text{whence } 3.\ P = X_2\left(\frac{AC \cdot w}{AB \cdot X_1}\right)$$

where AD, AC, and AB are distances in cm. along the lever; X_1 is the deflection in cm. caused by the weight on the rider; X_2 is the deflection in cm. caused by the measurement of capillary pressure; and P is the weight in grams pressing on the capillaries. To change P from weight in grams to pressure in grams per square centimeter, the right side of equation 3 is divided by the area of the glass (f) which is in contact with the finger. The equation then becomes:

$$4.\ \text{Pressure (gm./sq. cm.)} = X_2\left(\frac{AC \cdot w}{AB \cdot X_1 \cdot R}\right)$$

where R is the area in square centimeters of the glass (f). Since pressure in grams per square centimeter is equal to pressure in centimeters of water, to change the reading to millimeters of mercury pressure, the right side of the equation is divided by the factor 1.36.

The rider is so placed on the lever that AC equals AB, thus simplifying the formula. It now becomes:

$$5.\ \text{Pressure (mm. Hg.)} = X_2\left(\frac{w}{X_1 \cdot R}\right) \div 1.36$$

The quantities w and R are known and constant. In short, to calibrate the instrument at any time, the weight is placed on the rider, the amount of deflection caused is noted and by simple arithmetic a factor is found which when multiplied by the deflection obtained in measuring capillary pressure gives the pressure directly in mm. Hg. The instrument which is pictured herewith is calibrated so that each mm. on the scale equals 2 mm. Hg. pressure.

A reading is taken as follows. The patient is at rest in the sitting posture with his hand, well supported, at heart level, to obviate differences due to hydrostatic pressure. A drop of cedarwood oil is placed on the finger at the nail-bed. The finger is placed on the rest (e), and raised by means of the screw so that the glass (f) comes in contact with the skin at the nail-bed. By watching the movement of the lever on the scale, the point of contact is easily determined. The microscope is then focussed on the capillary bed through

the glass (b). Pressure is easily applied by means of the screw, raising the finger rest against the lever. The other hand manipulates the focus of the microscope. When the end-point is reached, the pressure applied is read off directly on the scale in mm. Hg. One person can easily make a reading.

Readings are taken on two or three capillaries in the same finger and the results averaged. The finger of choice, we find, is the ring finger, because it is usually the best preserved as far as the skin at the nail-bed is concerned. The procedure is repeated on the middle finger, and the results of both fingers are averaged as the mean capillary tension. With a little practice, the entire process need not take more than five to ten minutes.

As an end-point we use the initial slowing in a medium-sized capillary. Only the more superficial capillaries are used; that is, those which come into view first. Initial slowing is not a difficult end-point because appreciable slowing is rather sudden in occurrence. Flow does not seem to be impaired until a certain amount of pressure is applied, when an abrupt slowing takes place. The reasons for choosing the end-point we did are: (1) It is definite. Readings on the same capillary several times give almost identical results. During a pressure determination a point is reached when a slight increase in pressure applied causes a marked slowing in capillary flow. This point remains more or less constant in successive readings. (2) It is accurate. Pressure applied on the outside of a capillary has no effect on its caliber or flow until it equals the pressure within the vessel. When the latter situation occurs, the flow is hindered. Increased extravascular pressure hinders the flow progressively until complete cessation occurs. It is obvious, then, that the most accurate end-point is the initial change in rapidity of flow. As mentioned above, this change, fortunately, is rather sudden, thus making it available as a convenient and definite end-point.

The results obtained by Landis,[6] using the method of direct microinjection of capillaries, are probably the most accurate representations of true capillary pressure, as indicated above. The fact that our results correspond closely to his is an important bit of evidence that our instrument is accurate, and that our end-point is correct.

To determine whether the factor of skin elasticity played an appreciable part in indirect measurement of capillary pressure, we took readings on men and women with varying textures of skin at the nail-bed. Readings did not differ materially. This finding is in accordance with those of other investigators using indirect methods. (Danzer and Hooker[16]; Boas.[35])

Besides being very convenient, the fact that readings can be taken rapidly increases the accuracy of the results. Initial pressure applied falls on the superficial venous plexuses, causing a retardation of flow

and back-pressure to the capillaries, increasing the tension in the latter vessels. The greater the delay in raising the external pressure to that within the capillaries, the greater the back-pressure. The short time which is consumed in taking a reading with our instrument practically obviates this difficulty.

RESULTS

Readings were taken on fifty subjects. Of these, thirty were not hospitalized, and twenty were confined to the hospital for conditions unrelated to the cardiovascular, renal, or pulmonary systems. All the subjects had diastolic blood pressures between 60 and 80, and systolic blood pressures between 110 and 130 mm. Hg. The group consisted of forty males and ten females. The temperature of the room in which observations were made was about 20° C. Determinations were made on fingers which were normally warm.

An example of how results were tabulated follows.

P. M., normal white male, aged 24 years. Temperature of room—18° C. Fingers normally warm. Texture of skin soft. Blood pressure—124/76. Capillary pressure:

1. Ring finger:		
a. 1st capillary	22 mm. Hg.	
b. 2nd capillary	24	Average—22 mm. Hg.
c. 3rd capillary	20	
2. Middle finger:		
a. 1st capillary	24 mm. Hg.	
b. 2nd capillary	19	Average—21 mm. Hg.
c. 3rd capillary	20	

Mean capillary pressure: 21.5 mm. Hg.

Variations in readings on the same individual in different capillaries were slight:

5 cases showed a variation of 0-1 mm. Hg.
32 cases showed a variation of 2-3 mm. Hg.
13 cases showed a variation of 4-5 mm. Hg.

Results obtained in the series of fifty individuals were as follows:

20 per cent of the readings were 18-21 mm. Hg.
70 per cent of the readings were 22-25 mm. Hg.
10 per cent of the readings were 26-29 mm. Hg.

It will be seen that these results correspond closely with those obtained by Landis.

SUMMARY

1. Methods for the determination of human capillary pressure have been reviewed and criticism has been attempted from the viewpoints of accuracy and of clinical applicability.

2. A device is described which is easily applicable to routine clinical use. The results obtained fall well within those obtained by the

method of direct intubation of Landis, thus leading us to believe that they are substantially accurate.

3. The average capillary pressure, in the normal individual we find to be 18-29 mm. Hg.

The authors wish to express their appreciation of the efforts of Dr. Roger S. Estey, who carefully examined and corrected the physical principles of the instrument, and of Klett Mfg. Co. in New York City, who constructed the instrument.

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Department of Clinical Reports

CORONARY THROMBOSIS WITH COMPLETE HEART-BLOCK AND RELATIVE VENTRICULAR TACHYCARDIA A CASE REPORT*

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THOUGH Levine[1] states that with coronary thrombosis almost any form of cardiac irregularity may be found, he also states that one of the more uncommon occurrences is the development of complete heart-block. In the 145 cases of coronary thrombosis which he reports, complete heart-block was known to have occurred in but two cases. In one of these a ventricular rate of 28 was recorded. The ventricular rate of the other case is not given. He reports that paroxysmal ventricular tachycardia developed in five cases of this series.

Numerous cases of complete heart-block with ventricular tachycardias have been reported as developing in patients who were receiving massive doses of digitalis,[2, 3, 4, 5] and it has been generally accepted that the digitalis was a causative factor in the production of these ventricular tachycardias—of the ventricular tachycardias of the "supra-ventricular form" as well as of the paroxysmal form. However, in 1928, Carr and Reddick[4] reported a case of complete heart-block with an auricular rate of 110 and a ventricular rate of 83 in a young woman, with mitral disease and acute arthritis, who had not received digitalis. Other and similar though less definite cases have been reported, but without statements as to digitalis medication. It therefore seems possible that relative ventricular tachycardia may not be of rare occurrence in cases of complete heart-block where digitalis can be entirely excluded as a causative factor. Such a case is here reported.

CASE REPORT

A practising physician, 56 years of age, who for many years had considered himself to be in perfect health, was taken suddenly, while driving home to lunch, with an agonizing pain in the region of the lower part of the sternum. He was able, however, to control his automobile until he reached his home, which was but a short distance away. His wife helped him from the street to the house and saw that he was very ill. About this time he began to vomit, and he fell to the floor as he entered the house. A neighboring physician was at his side in a few moments. This physician carried the sick man to a bed and thought that he was dying. His radial pulse was not palpable and his heart sounds were very faint.

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I was called to the sick man's bedside about thirty minutes after the onset of the attack. He lay propped up on pillows, between wide open windows. It was very evident that he was in extreme shock and in great distress; his color was ashen and he was drenched with sweat. However, he had no notable dyspnea. His complaint was of an agonizing pain which centered behind the lower part of his sternum and extended to both arms. He said that the pain in the arms was even

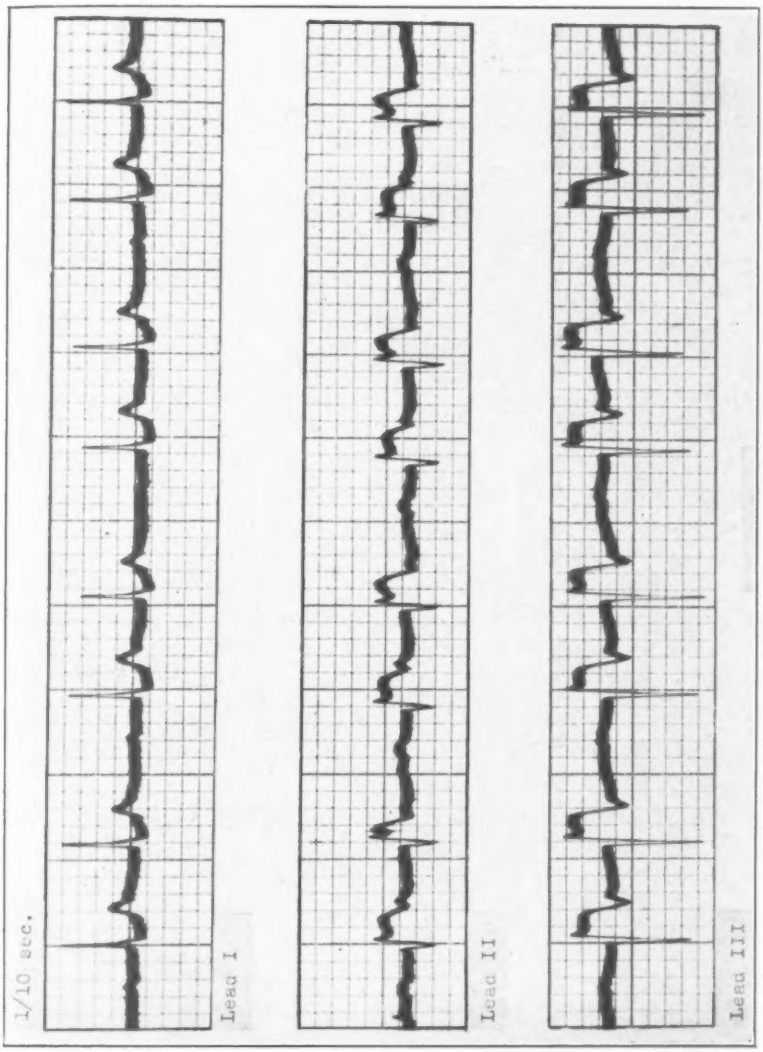

Fig. 1.

more severe than was the pain in the region of the sternum. The radial pulse was now 44 and quite regular, but very soft. The heart sounds were faint, but the ventricular rate was the same as that of the radial pulse. It was, however, observed at this time that the visible impulses of the external jugulars seemed to have twice the rate of the arterial pulse.

One or more nitroglycerin tablets had already been given, with no relief. After the contents of several ampules of amyl nitrite had been inhaled to no effect, a

quarter of a grain of morphine was given hypodermically. The morphine controlled the pain rather well. He slept a little and then remained quiet for about two hours. From that time morphine was given freely in the attempt to control the pain which continued to be severe. For some five or six hours, throughout the afternoon, the pulse remained at 44 and the rhythm continued quite regular. The pulse became much stronger and the heart sounds became somewhat clearer as the

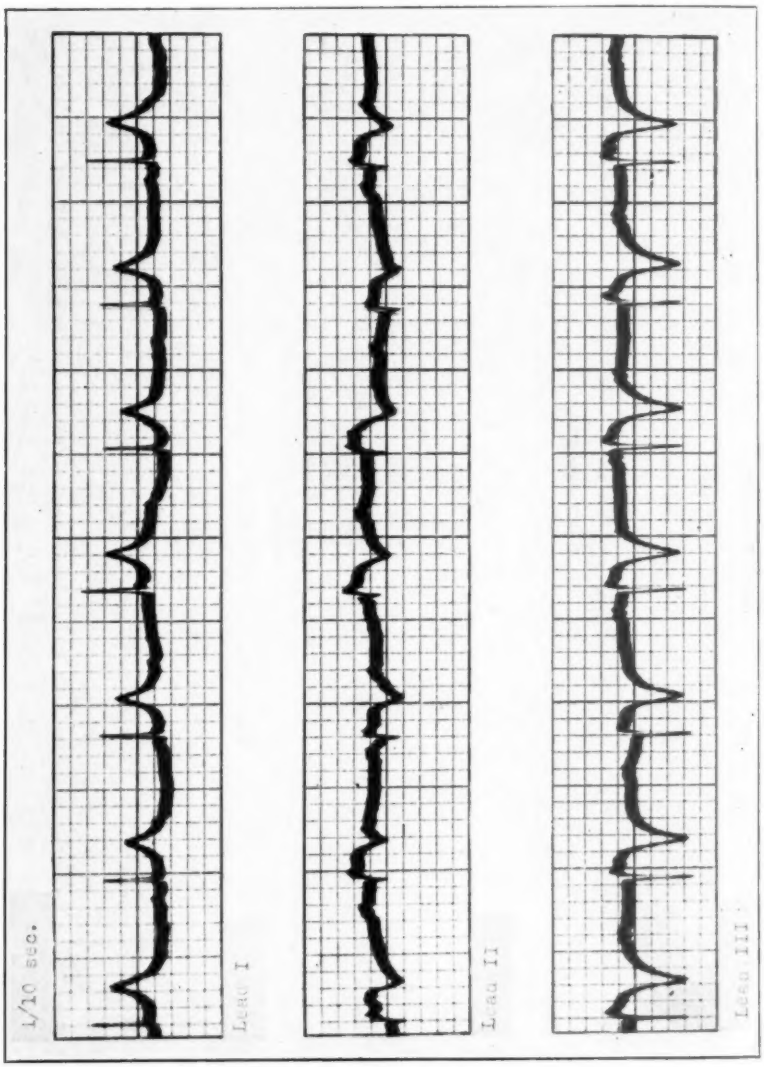

Fig. 2.

and there were occasional dropped beats at irregular intervals.
afternoon advanced. Early in the evening, the pulse rate increased to about 70

Though the sick man had morphine during the night, he rested very badly, and his chest and arm pains were very distressing. He was taken to the hospital early the next morning and electrocardiographic records (Fig. 1) were taken at 9 A.M. The electrocardiograms showed an advancing, 3-to-2 heart-block, together with the

characteristic evidences of coronary thrombosis. A leucocyte count was reported as 12,000. At 3 P.M. the temperature was 99°; in the evening it was higher. All later temperature records showed elevations above normal. On the morning of the second day in the hospital the leucocyte count was 16,000. A blood Wassermann was reported negative. The second electrocardiographic records (Fig. 2) were taken on the morning of the second day in the hospital. These electrocardiograms showed complete heart-block with an auricular rate of 120 and a ventricular rate of 70, each rate being quite regular.

During the patient's second day in the hospital, to-and-fro pericardial friction sounds were heard. He complained now of severe pain in his neck, in addition to the chest and arm pains. He was also much distressed by abdominal "gas pains," and his respirations were labored. He grew steadily worse and died at 7:30 A.M., the third day in the hospital.

This patient received no digitalis or any other heart stimulant prior to or during his final illness.

Autopsy.—The body was that of a small man, 56 years of age. The pericardial fluid was slightly increased and cloudy. A thin, shaggy layer of fibrinous material was attached to the anterior surface of the heart. The major portion of that area which represented the surface of the right ventricle showed the dark purplish discolorations characteristic of infarction. The heart weighed 260 grams. The cardiac valves were all quite normal. No mural thrombi were found. The infarction seemed to involve the greater portion of the outer wall of the right ventricle, recent, degenerative changes being found by section to extend to the apex and to the interventricular septum, both anteriorly and posteriorly. No definite, degenerative changes were found involving the left ventricular myocardium. No fibrous areas suggestive of old myocardial lesions were found. The aorta was smooth and quite free from atheromatous changes. The coronary openings were unobstructed. However, on dissection of the right coronary artery, it was found to be much thickened, hard and slightly nodular, though the lumen seemed to be unobstructed for the first 2 cm. Then, a recent, dark thrombus was encountered. This thrombus was traced well into the infarcted myocardium. On dissection of the left coronary artery the walls were found to be remarkably soft and normal in appearance, no sclerotic changes being evident.

COMMENT

Clinical observations made soon after the onset of the attack led to the impression that a 2-to-1 heart-block was present. It seemed that after a few hours the conduction improved to the extent that only an occasional auricular impulse failed to bring a response from the ventricles. On the second day conduction was progressively failing. On the third day complete A-V disassociation was present with a ventricular rate far in excess of that which is commonly assumed to be the inherent rate of contraction of the ventricular myocardium.

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AURICULAR FLUTTER IN A NEWLY BORN INFANT*

Report of a Case

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AURICULAR flutter is an infrequent event in children. In 1929 Willius and Amberg[1] reviewed the literature of paroxysmal tachycardia in children. They found reports of only six cases of auricular flutter. The youngest patient in the latter group was an infant of three months. Sir Thomas Lewis[2] reported the case in 1915. We have found no reports of other cases of flutter in children since the publication of the paper of Willius and Amberg.

Dressler and Löwy[3] believe that many of the cases reported as auricular paroxysmal tachycardia are in reality cases of flutter, and make this statement: "The reports of cases in which no graphic registration is included appear to justify the opinion that here we are usually dealing with flutter, inasmuch as the pulse frequency observed in these cases is often of such a height (220-260) as is commonly found only in flutter." Even though this surmise may be correct the incidence of flutter in childhood is far from common.

In this connection, reference should be made to the cases of paroxysmal tachycardia reported by de Bruin[4] and by Doxiades[5] since Willius and Amberg published their paper. De Bruin's case was one of paroxysmal tachycardia in an infant of five weeks. The cardiac rate was 280. An electrocardiogram was not obtained. Doxiades reported four paroxysms of tachycardia in an infant beginning when the patient was seven days old. In the second attack the rate was 240. The electrocardiogram was interpreted as that of an auricular tachycardia, but it is significant that the rate after the subsidence of the attack was half that of the rate during the paroxysm.

The case which we are reporting is the first, so far as we can find, in which the flutter was present at birth. The cardiac irregularity was noted occasionally before birth.

REPORT OF CASE

A white female infant, weighing 10 lb. 13½ ounces, was born at term by cesarean section on October 29, 1930. Dr. Charles E. Galloway, the obstetrician, states that the mother had had periods of uterine bleeding during early pregnancy which necessitated her remaining in bed most of three months (February 28 to June). During frequent examinations up to September 16 no abnormal fetal

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heart sounds were noted. On October 7 the fetal heart tones were very irregular, of a variable type which was unlike any other fetal heart irregularity which he had ever heard. Dr. Galloway considered it an exaggerated sinus arrhythmia. During uterine contractions of labor, the irregularity became accentuated and at times the heart tones could scarcely be heard. Following rupture of the membranes, the heart tones were not heard for about five minutes. When labor had lasted thirty hours, with complete dilation of the cervix but without engagement of the head, and with the fetal heart sounds irregular, cesarean section was done.

On September 30, Dr. Philip H. Smith found the fetal heart rate about 160 per minute with some irregularity of a constant type. On two occasions during

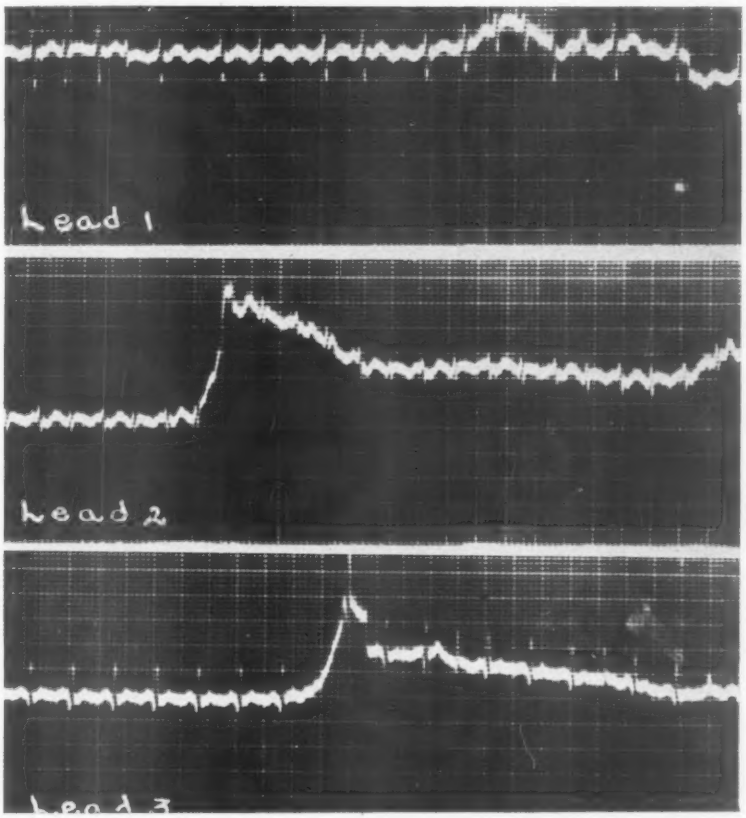

Fig. 1.—Electrocardiogram taken October 30, 1930, about twenty-six and one half hours after birth. Note flutter, with irregular block in Lead I.

labor he examined the fetal heart and noted a marked variable irregularity which he interpreted as sinus arrhythmia. This irregularity was different from that which is often heard at the end of the second stage of labor when the baby is in distress.

At birth, at 8:16 A.M., October 29, because breathing was somewhat slow in starting, resuscitative measures were used, after which the baby's color was good.

The infant was first seen by one of us (McClure) at this time, about six minutes after birth. The respiratory movements were rapid. The heart beats were about 180 a minute, with marked arrhythmia at times; there were also short periods of a much more rapid rate, and of a much slower one. No murmur was heard, and except for the abnormal heart action and rapid breathing, the infant seemed normal.

At 5:30 P.M. the respiratory rate was 60 a minute. The heart rate and rhythm were still variable and were definitely influenced by the deeper respiratory movements.

At 9:30 A.M., October 30, the heart sounds were regular for longer intervals with the rate between 188 and 192 a minute. When the infant held her breath momentarily before crying, there was a marked slowing with a gallop-like rhythm for a few beats, with a return to regular, rapid beats when she relaxed. The baby had regurgitated dextrose solution feedings during the night.

At 5:15 P.M., October 30, while the infant was sleeping, the respirations were 65 a minute and the heart sounds which were regular, were 192 a minute. Irregularity occurred only when she was awake and crying.

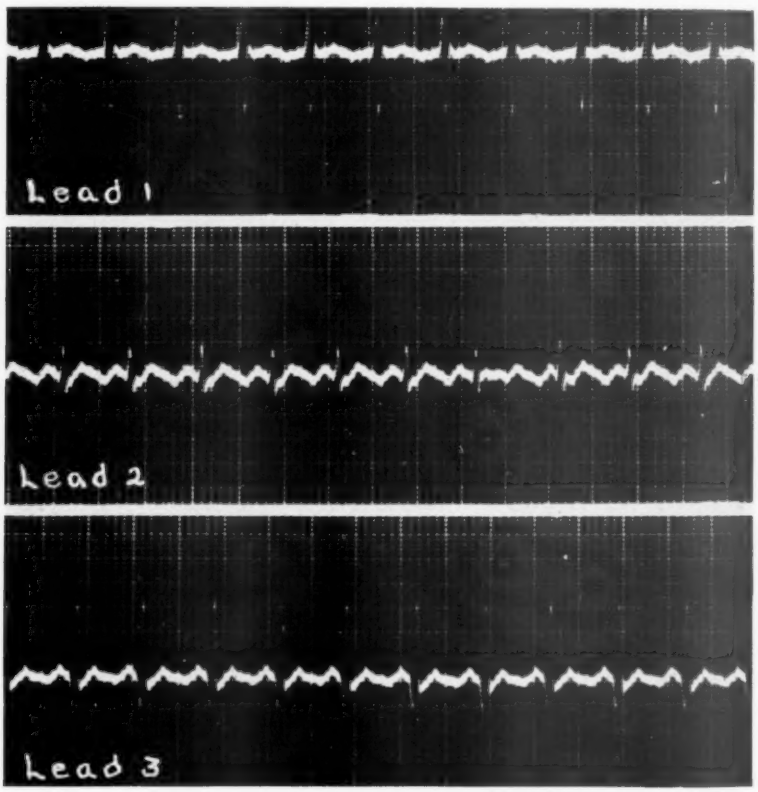

Fig. 2.—Electrocardiogram taken October 31, 1930, with motor speeded up. Flutter with 2-1 rhythm: 3-1 noted once in Lead II.

At 10:45 A.M., October 31, the infant's color was good. The heart beats were 192 a minute, becoming irregular when the child moved and made sounds. The respiratory rate was 60 to 64 a minute. During the previous night, on two occasions, the baby had manifested cyanosis about the mouth and face.

During the first three days of November, on several occasions there was slight cyanosis. The baby regurgitated a number of times and cried considerably. There was no significant change in the heart action. During November 4 to 7 inclusive, the baby appeared well but the heart action remained the same. There was slight cyanosis only when the infant cried. She had been considerably more fretful and restless than is usual at this age.

On the morning of November 8, the child was no longer fretful and restless and had slept all night. On examination at 11:15 A.M. the heart rate was 144 a minute and the irregularity previously found on crying was no longer present. Subsequent examinations have revealed only normal heart action.

A systolic murmur, indefinite on examination of November 16 and 30, 1930, and January 3, 1931, was heard faintly but definitely on February 1 when the child was unusually quiet. This murmur was systolic, heard loudest over the base of the heart to the left of the sternum and faintly somewhat beyond the borders of the heart. The heart rate varied from 132 to 144 a minute with a normal rhythm. There was a slightly bluish tinge to the normal pallor about the mouth; the

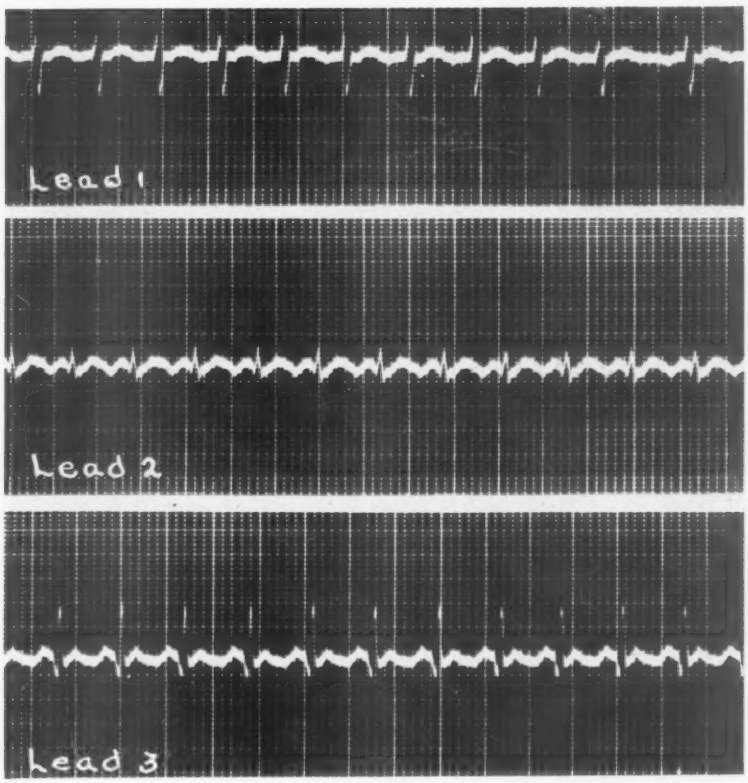

Fig. 3.—Electrocardiogram taken November 5, 1930. Flutter with 2-1 rhythm: 3-1 noted once in Lead I.

cheeks were somewhat flushed and the color of the skin was good elsewhere. There was no cyanosis when the child cried.

X-ray examination on the afternoon of October 29, 1930, showed during inspiration, an upper mediastinal shadow of about 70 per cent of the width of the heart shadow. Dr. James T. Case, from roentgenologic studies, was of the opinion that there was an enlarged heart and thymus.

X-ray treatment for the thymus was given by anterior exposure on October 30, and by posterior exposure on October 31, and by both anterior and posterior exposures on November 28. Fluoroscopic examination of the heart on November 7 gave little additional information except to confirm the rapid heart beat. X-ray

examinations on November 8 and 28, 1930, and January 31, 1931, showed no definite evidence of enlargement of the thymus. The heart apparently was a little larger than normal.

When last examined, on March 8, 1931, the infant weighed 18 lb. 4½ ounces and was doing well. The heart action was normal. A slight systolic murmur was heard with difficulty. There was no cardiac irregularity and no cyanosis with crying.

Fig. 4.—Electrocardiogram taken November 8, 1930. Normal mechanism. Rate 142.

SUMMARY

The important features in this case were: (1) a marked cardiac irregularity of a variable type which was noted *intra utero* during the last month of gestation; (2) after birth, a tachycardia with a rate of 180 to 192 beats a minute with periods of marked irregularity involving both rate and rhythm of the ventricular beat—the deeper respiratory movements, as with crying, markedly influenced these irregularities; (3) return to normal of the heart rate and rhythm on the tenth day after birth, with no recurrence of the abnormality; (4) establishment of the diagnosis of auricular flutter by electrocardiogram made about twenty-six and one-half hours after birth.

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Department of Reviews and Abstracts

Selected Abstracts

Barcroft, Joseph, and Izquierdo, J. J.: The Relation of Temperature to the Pulse Rate of the Frog. J. Physiol. 71: 145, 1931.

The object of the present paper was by a comparative study of the temperature coefficients of the hearts of certain cold and warm blooded animals to gain further knowledge of the point at which the nervous system commences to dominate the response of pulse rate to temperature and, if possible, to ascertain the nature of the nervous control if such were found to exist. It deals with the effect of temperature on the pulse rate of the frog.

The excised frog's heart studied in winter time usually gives a linear relationship between the logarithm of the frequency of the sinus beat and the reciprocal of the absolute temperature between 5° and 20° C.

The value of Q_{10} varied in the minority of cases, as the temperature rose the frequency decreased as compared with the above relationship. In the intact frog in winter the results were irregular.

The excised heart of the frog in summer showed a different property. The frequency bore a nearly linear relation to the temperature. This was true also of the heart of the intact frog. The relation of the frequency to the temperature was little if at all, influenced by doses of atropine of the strength which just sufficed to block the vagus.

Barcroft, J., and Verzár, F.: The Effect of Exposure to Cold on the Pulse Rate and Respiration of Man. J. Physiol. 71: 373, 1931.

Apart from spasmodic rises in the pulse rate associated with shivering, the pulse rate in man falls with fall of body temperature. The spasmodic rises associated with shivering may amount to 40 per cent of the original pulse rate.

The respiration shows marked summation of inspiratory movements during the rigors which had very deep and sustained inspirations. The oxygen consumption increases during the shivering fits by as much as 75 per cent of its value during rest.

Patten, Bradley M.: The Closure of the Foramen Ovale. Am. J. Anat. 48: 19, 1931.

The author has studied hearts of over one hundred and sixty infants, ranging from newborn to the second year of age with especial reference to conditions at the foramen ovale. The cases were consecutive in the sense that they included every workable case which could be examined at first hand during the past three years. As a result of this study, the following summary is presented.

The abandonment of the foramen ovale as an equalizing short cut between the right and the left atrium is not an abrupt but a gradual process. At the close of embryonic life the pulmonary circulation is of sufficient volume to care for oxygen intake and carbon-dioxide elimination, so that there is no necessity of

assuming any revolutionary change in the course of blood through the heart at the instant of birth. Under the influence of the functional activity of the lungs, the pulmonary flow undergoes a smooth steady rise during the first few weeks after birth. The progressive diminution in the bore of the ductus arteriosus is concomitant and indicative of the postnatal increase in volume of the pulmonary circulation.

As the pulmonary circulation increases there is less compensatory flow through the foramen ovale from the right to the left atrium. This reduction in flow is evidenced anatomically by a parallel reduction in the fullness of the valvula foraminis ovalis, and the consequent diminution of the functional orifice to a progressively narrower slit between the valvula and the septum. This first phase in the closure of the foramen ovale occupies approximately the first postnatal month during which time the pulmonary return is mounting to equivalence with the right atrial intake. Although a probe can still be passed freely behind the valvula, the foramen ovale may be regarded as functionally closed when this new intracardiac balance has been attained and the valvula lies tightly against the septum.

Then follows a period of six to eight months in which the connective tissue of the valvula increases from 600 to 700 per cent. Probe patency still persists but the size of the slit through which a probe may be passed progressively diminishes and the resistance to its passage increases with the increase in the thickness of the valvula. This second phase in the closure of the foramen ovale with its characteristic histological alteration is essentially the conversion of an originally movable flap-like valve into a fixed septal structure.

Finally, coming leisurely in the wake of functional abandonment and as a culmination of the period of connective-tissue proliferation, is the adhesion of the valvula to become an integral part of the interatrial septum. There is great individual variability in the age at which this final step in the obliteration of the foramen ovale occurs. A usual range rather than a specific time of final anatomical closure is all that can be specified. Substantiated cases of complete fibrous adhesion of the valvula to the septum under three months are exceedingly rare. The usual time of complete anatomical closure appears to be not earlier than the last third of the first year after birth and is frequently much later.

Mere failure of the completion of the fibrous union of the valvula with the septum should be sharply distinguished from the frankly abnormal conditions in which the foramen ovale remains inadequately guarded. Incomplete adhesion with "probe patency" is so common that it must be regarded as a variant of the normal rather than as an abnormality. Approximately 25 per cent of all adult hearts show it in some degree. As long as the valvula foraminis ovalis adequately overlaps the limbus fossae ovalis, probe patency is no functional handicap to an otherwise normal individual.

Borman, Milton C., and Meek, Walter J.: IV. Coronary Sinus Rhythm. Rhythm Subsequent to Destruction by Radon of the Sino-Auricular Nodes in Dogs. Arch. Int. Med. **47**: 957, 1931.

The authors in this study have tried to determine the exact site of the initiation of the cardiac impulse in dogs in which complete destruction of the sino-auricular nodes had been produced by radon. Twenty-one animals were studied. The previous observation that the nodal tissue of the coronary sinus apparently acts as a reserve mechanism, as a pacemaker under conditions of experimental destruction of the sino-auricular node is corroborated.

Evidence is presented that suggests that a coronary sinus rhythm cannot be differentiated from a sino-auricular rhythm by means of an electrocardiogram.

If the sino-auricular node is destroyed gradually by radon, the nodal tissue of the coronary sinus assumes the function of pacemaker. It is probable that when the

sino-auricular node is rendered functionless by disease the nodal tissue of the coronary sinus acts as pacemaker. Permanent nodal rhythm cannot be produced by destroying the sino-auricular node with radon.

The electrocardiographic changes in dogs following the destruction of the sino-auricular nodes by radon are: temporary reduction of the P-R interval which later becomes normal, slightly greater or slightly less than normal; decreased cardiac vagal tone; partial and complete sino-auricular block; partial and complete auriculo-ventricular block; nodal rhythm; coronary sinus rhythm; inverted T^2 and T^3 and premature ventricular beats.

Izquierdo, Jose Joaquin: Experimental Evidence of the Controlling Action of the Aortic and Carotid Sinus Nerves Upon the Rises of General Blood Pressure. Arch. Latino Amer. de Card. y Hemat. **1**: 193, 1931.

Comparison of the blood pressure curves obtained by stimulating the peripheral end of the splanchnic nerves by a constant cardiac stimulus under similar conditions, first with the two sets of aortic and carotid sinus nerves intact and then with these nerves partially or totally eliminated, was made in connection both with their maximal height, measured in mm. Hg, and with their form, specially the variations of the "step" or "dip" which occurs shortly after the beginning of the rise. The following results were obtained:

1. In the normal condition, the height reached by the splanchnic pressure curve is notably reduced by the action of the aortic and carotid sinus nerves, particularly the latter.

2. The typical and constant feature in the normal splanchnic pressure curve is related to the activities of the aortic and carotid sinus nerves, particularly the latter.

3. The two carotid sinus nerves and the two aortic nerves alone, are capable of exerting the same inhibiting effect upon the height and of producing the "dip" in the splanchnic pressure curve. Of the two pairs of nerves, the sinus nerves are those which exert the more important inhibitory effect.

4. When a single carotid sinus nerve is left active its effects upon the height and form of the splanchnic pressure curve are often considerable.

5. Tying off of both adrenals at the beginning of the experiment or after partial or total suppression of the aortic and carotid sinus nerves does not modify the results in the rabbit, the hare and the dog. But in the cat the "dip" more frequently disappears after the ipsilateral gland is tied off.

6. These two variations, namely in the height and "dip" in the curve are due to reflexes originating in the blood pressure receptors in the aortic and carotid sinus walls.

7. Both series of changes are compatible with the view that the rise of blood pressure produced by stimulation of the splanchnic nerve represents the balance between two factors working in the opposite direction, (2) the direct vaso-pressor effect (vasoconstriction in the splanchnic area), and "b" the indirect vaso-depressor effect (aortic and more especially carotid sinus reflexes) evoked by the rise of blood pressure.

Chillingworth, Felix P., Haskins, Frank E., and Casey, Gertrude U.: Assay of Tinctures of Digitalis. Jour. Lab. & Clin. Med. **16**: 850, 1931.

The object of this survey was to determine to what extent tincture of digitalis as dispensed in representative drug stores of metropolitan Boston conformed in strength to the standard laid down as official in the United Stated Pharmocopea. Although this is strictly speaking a local survey, the results are none the less of general interest owing to the fact that more than seventy-five per cent of the

tinctures assayed are the products of commercial pharmaceutical houses whose tinctures of digitalis are depended upon by practiced physicians throughout the country.

Eleven per cent of the tinctures assayed were above the U. S. P. requirements. In cases where massive doses are indicated, such over strength is especially dangerous. This percentage could not be explained by frog seasonal variation.

The evidence offered by this survey indicates that the variation in potency found in the tinctures varied less than that showed by other similar surveys. The authors believe that further improvement will take place when all manufacturers market their tinctures in sealed one-ounce bottles giving an expiration date.

Powers, John H., Pilcher, Cobb, and Bowie, Morris A.: Some Observations on the Circulation in Experimental Mitral Stenosis. Am. J. Physiol. **97:** 405, 1931.

The purpose of this report is to present observations on the cardiac output of 5 dogs with experimental mitral stenosis. Since the animals had been utilized previously for some work on the blood volume of normal dogs, these studies were repeated after the development of mitral stenosis and are included. Alterations in cardiac size as demonstrated by roentgenological examination are also recorded.

The present consensus of opinion concerning heart disease in general favors the premise that the cardiac output per minute is decreased in proportion to the extent of cardiac damage. Experimental evidence to support this contention, however is extremely fragmentary and is not sustained by the results of these investigations.

The cardiac output of 4 of the animals ranged between 104 c.c. and 230 c.c. per kilogram per minute; the average was 170 c.c. These figures are within the range of normal. The output of the fifth animal was distinctly elevated being 323 c.c. per kilogram per minute.

The basal pulse rate was increased in four instances and normal in the fifth. The blood pressure was elevated in only one case. An increase in the percentage of red blood cells occurred at the expense of the plasma. No significant changes were observed in the electrocardiographic tracings. Observations on the control animal showed no variations from the normal.

The size of the heart as determined by the roentgen shadow showed a progressive enlargement in all five dogs.

Katz, L. N., and Wallace, A. W.: The Role of Cardiac Ischemia in Producing R-T Deviations in the Electrocardiogram. Am. J. M. Sc. **181:** 836, 1931.

The three cases reported indicate that acute myocardial ischemia depends not only on coronary occlusion and pericardial effusion but also on the competence of the heart and its dilatation. They also illustrate some of the errors liable to creep into the interpretation of the significance of the so-called "coronary R-T deformities." These observations substantiate the findings that coronary occlusions can be produced in normal animals without changing the R-T segment of the electrocardiogram. It was observed that such changes in the R-T segment ensue when the myocardium becomes incompetent.

Hurxthal, Lewis M.: The Clinical Significance of Abnormalities of the Electrocardiographic Complexes. New England J. Med. **205:** 95, 1931.

The author describes in abstract form the usual interpretations passed on abnormalities of the various complexes of the electrocardiogram. Suitable electrocardiograms are published to illustrate the various points mentioned.

Drake, E. H.: The Use of the Electrocardiograph in the Study of Cardiac Arrhythmias, Bradycardia and Tachycardia. New England J. Med. **205**: 92, 1931.

The author reviews briefly the important points observed in electrocardiograms from patients with these cardiac disturbances of mechanism.

Faulkner, James M.: Methods of Electrocardiography and the Normal Electrocardiogram. New England J. Med. **205**: 88, 1931.

This brief presentation of the principles underlying electrocardiography and the description of the string galvanometer and the normal electrocardiogram gives a good idea of this field of physical examination. The brevity and clearness of the article makes it of value to beginners in the subject.

Sproull, John: Roentgen Study of the Thoracic Aorta. New England J. Med. 205: 83, 1931.

The author describes the findings of the heart and great vessels on roentgen examination and then briefly summarizes the common conditions producing changes in the aorta and their characteristic attendant roentgen changes.

Sosman, Merrill: Roentgen Study of the Heart. New England J. Med. **205**: 80, 1931.

The author as a roentgenologist states that it is possible to assist in cardiac study in three ways: (1) by determining the exact size and shape of the heart and by making permanent records for future comparison; (2) by obtaining an idea through fluroscopic examination as to the character of the heart beat and the condition of the myocardium; (3) by identifying isolated conditions such as aneurysm, calcified pericardium, Hodgkins disease and other mediastinal tumors.

Rösler, Hugo: Methods of Cardiovascular Study by the Roentgen Ray. New England J. Med. **205**: 77, 1931.

The chief value of cardiovascular x-ray examination is in the case of the following conditions: (1) emphysema, thick or deformed chests and other thoracic diseases; (2) dilatation of the left auricle; (3) calcification and dilatation of the descending aorta; (4) thickening and calcification of the pericardium; (5) malformations; (6) diseases of the pulmonary arteries; (7) lung stasis in cardiac decompensation; (8) luetic aortitis.

The author describes the usual method employed in undertaking x-ray examination. Particular emphasis is placed on the value of fluroscopic methods for observing the motion of the heart. Orthodiograms and teleroentgenograms are also described. Mention is made of the value of plates made in oblique positions of the chest. Mention is also made of the use of barium mixtures for studying the relationship of the esophagus, aorta and pericardium.

Grimes, Eli: Effect of Intrathoracic Pressure on Arterial Tension. Arch. Int. Med. **47**: 876, 1931.

The author states that if a person shuts off the outlet of air by closing the larynx or nose and lips and makes a forced expiratory effort the intrathoracic pressure rises and the blood cannot flow into the chest; hence the right side of the heart does not fill, the blood is soon pumped out of the lungs and the left ventricle likewise becomes empty, arterial circulation is momentarily suspended and the systolic blood pressure falls to zero. After the systolic pressure has fallen, respira-

tion is resumed and the systolic pressure rises from 50 to 150 above the patient's normal pressure. This rebound depends on the amount of blood, the elasticity of the arteries and the contractile force of the heart. Other conditions being constant the elevation in pressure is in inverse ratio to the elasticity of the arteries, therefore, the respiratory rebound is a measure of the elasticity of the arteries.

A high respiratory rebound is the first indication of oncoming hypertension and of arterial fibrosis with or without high pressure. A person showing a high rebound should be intensively studied for syphilis and nephritis. The test does not indicate the integrity of the heart, measure its efficiency or foretell its failure.

De La Chapelle, Clarence E., and Graef, Irving: Acute Isolated Myocarditis. Arch. Int. Med. **47**: 942, 1931.

A case of so-called myocarditis of unknown etiology is reported. Clinical and necropsy observations are compared with those in previously recorded cases.

Progressive heart failure was the outstanding clinical feature. The embolic phenomena noted during life and the evidence for the same found at necropsy are particularly noteworthy and possibly give a clue to the onset and duration of the lesion. The cerebral accident about eight and one-half months before death, the healed infarct in the kidney and the probable pulmonary infarct about six weeks before death suggest that the intracardiac thrombi were present for some time. The heart weighed 600 grams and exhibited marked hypertrophy lending further support to the contention that the disease had existed for a period of months.

The diffuse and focal cellular infiltration consisting chiefly of lymphocytes, the new formation of blood vessels and connective tissue involving both the interstitium and the parenchyma, the well-marked deposits of organized connective tissue and the focal areas of necrosis account for the progressive circulatory failure. There were no vascular, perivascular or myocardial lesions suggestive of rheumatic infection and no Aschoff bodies were found. Electrocardiograms gave further evidence of the extensive distribution of the lesion.

Willius, Fredrick A.: The Heart in Old Age. A Study of 700 Patients Seventy-Five Years of Age and Older. Am. J. M. Sc. **182**: 1, 1931.

This study is based on 700 patients 75 years of age and older who were carefully investigated at The Mayo Clinic from August, 1914, to January, 1930, with special reference to the cardiovascular system. This group represented an incidence of 1.1 per cent of persons who had undergone electrocardiographic examinations.

The ages of the patients ranged from 75 to 96 years. Forty-seven per cent of the patients were aged 75 and 76 years. The numbers in the various groups diminished progressively with advance in age; only 0.5 per cent were between the ages of 91 and 96. The ratio of the sexes was 5 men and 1 woman. Seventy and three-tenths per cent of the patients had systolic blood pressure of 140 mm. or more; only 9.7 per cent had systolic blood pressure of 200 mm. or more. The mean blood pressure ranged from 109 to 127.8 mm. The diastolic pressure of 110 mm. or more occurred in 107 cases. Pulse pressure of 60 mm. or more occurred in 69.6 per cent of cases and readings of 90 mm. or more in 20.7 per cent. It is evident from this study that hypertension is the rule in aged patients. There were 315 patients without clinical evidence of heart disease as opposed to 385 patients with clinical evidence of heart disease.

From this study of aged patients, one gleans the impression that the majority of persons even in the presence of evident heart disease, possess hearts of unusual quality. This impression becomes strengthened by the fact that only 85 patients had congestive heart failure. The heart impaired or unimpaired by disease that permits continuation of life to and beyond the seventy-fifth year is an organ of unusual quality.

Reinhart, Alfred S.: Evolution of the Clinical Concept of Rheumatic Fever. New England J. Med. **204:** 1194, 1931.

The author traces the history of rheumatism through the ages and stresses that portion of it which depicts successive recognition of the protean manifestations of rheumatic fever from the point of view of the historical evolution of the present concept of the disease. References to the literature are frequent and many important historical contributions are listed, particularly the early contributions describing the unusual features of rheumatic fever.

The author believes that the extra articular and the extra cardiac manifestations of rheumatism have been receiving increasing attention and recognition, and that the apparent clinical rarity of some of these manifestations will become less marked as clinicians pay more especial attention to and look more carefully for their presence. He points out the important fact that there is a changing conception of the disease from a local affection to a generalized affliction.

Boas, Ernst P.: Rheumatic Fever in Adult Porto Rican Immigrants. Am. J. M. Sc. **182:** 25, 1931.

The author has studied native Porto Ricans admitted to Mount Sinai Hospital with rheumatic fever. Nine of the cases were severe and were similar to the type usually seen in childhood. This observation suggested that the increased virulence of the disease might be explained by the absence of rheumatic infection in Porto Rico results in a greater susceptibility of Porto Ricans on exposure to the disease in the United States where rheumatic fever is endemic.

Registration of deaths shows that rheumatic fever and rheumatic heart disease are very rare in Porto Rico. From the records available, the author has determined that rheumatic infection is not very common among Porto Ricans who have immigrated to New York City.

Clawson, B. J.: Experiments Relative to a Possible Basis for Vaccine Therapy in Acute Rheumatic Fever. J. Infect. Dis. **49:** 90, 1931.

The purpose of these experiments was to learn whether or not there may be an experimental basis for vaccine therapy in patients having acute rheumatic fever. Starting with the fact that there is a similarity between the state of allergy toward streptococci in patients with acute rheumatic fever and that in animals made hypersensitive to streptococci experimentally and with the fact that hypersensitized animals can be desensitized, the author attempted to desensitize hypersensitive animals by means of intravenous vaccination.

The development or the non-development of subcutaneous nodules was used in the detection of hypersensitiveness or desensitization respectively. If the development of these nodules can be prevented in animals it was considered possible that by a similar method to desensitize patients having acute rheumatic fever and to prevent further development of lesions.

It was found that rabbits made hypersensitive to streptococci can be desensitized by such intravenous administration of a streptococcic vaccine. Injections of doses of streptococci that produced marked lesion in hypersensitive animals have little or no effect on vaccinated hypersensitive animals. This protective phenomenon is not strictly type specific but seems probably species specific. Protection is uniformly associated with a high titer of agglutination while hypersensitiveness is not. From experiments reported in this paper the possibility of the use of intravenous vaccine treatment in patients with acute rheumatic fever is suggested.

Wilson, May G., and Swift, Homer F.: Intravenous Vaccination with Hemolytic Streptococci. Am. J. Dis. Child. 42: 42, 1931.

The present investigation covers a period of observation of four years on a total of one hundred and seventy-two children attending the Heart Clinic of the New York Nursery and Child's Hospital. Approximately one-half of the children received intravenous vaccination and the remaining number, a comparable group, were observed as control series. The vaccine used was prepared at the hospital of the Rockefeller Institute. It consisted of a heat-killed culture of hemolytic streptococcus strain Q 33 suspended in 0.5 per cent phenolized physiologic solution of sodium chloride so that 1 c.c. represented the required dose. The first injection consisted of 250,000 micro-organisms and each subsequent weekly injection contained double that of the preceding one until the maximum of 10,000,000 was reached and this dose was repeated until a total of from nine to twelve treatments had been given.

The incidence of recurrence and manifestations of activity in both groups was comparable during two years, 1927-28 before vaccination was given. The yearly incidence of recurrence in the treated group was less than in the control group during the two years 1929-30 after treatment. Forty-five per cent of the treated children as compared with 18 per cent of the controls were free from recurrence for periods of from sixteen months to two years after treatment.

The causal relation of intravenous vaccination with hemolytic streptococcal vaccine to the diminished incidence of recurrence observed is discussed. Final judgment as to the causal relation must await the results of further investigation. It would seem best at the present time to restrict the therapeutic application of intravenous vaccination in rheumatic children to control investigation.

Selkirk, Theodore K., and Mitchell, A. Graeme: Evaluation of the Results of Tonsillectomy and Adenoidotomy. Am. J. Dis. Child. 42: 9, 1931.

This study follows the methods commonly employed by other investigators in studying the effects of tonsillectomy and adenoidotomy and includes one hundred and thirty children who had had operation. The authors analyze the physical findings and symptoms in this group of children subsequent to operation as compared with those previous to operation. In this series there were ten cases of rheumatic infection. The incidence of attacks of joint pains following operation is not stated in this article. In general, it was noted in this study that three years after tonsillectomy and adenoidotomy there was a lessened incidence of colds, nasal obstruction and sore throat while sinus infection, headache and growing pains were increased in frequency.

This paper is concerned chiefly with the statement of the difficulties surrounding the whole problem. The authors feel that this study of the after results of the operation has added to their doubts of the possibility of analyzing satisfactorily their own personal observations and has increased their skepticism of the conclusions drawn from many of the studies made by others. They believe that no attention, or too little attention has been paid to certain modifying factors, principally age, sex, race, heredity, financial class, season, effect of adenoidotomy alone, length of observation after operation, source from which the history and other data are obtained, incidence of tonsillectomy in the community at large and the suitability of the control group.

They state that many of the symptoms and conditions popularly supposed to be associated etiologically with diseased tonsils are those in which the natural course and incidence regardless of the tonsillectomy are not known. It would seem that the conclusions drawn from some of the studies which are widely quoted as showing the effects of tonsillectomy are decidedly open to question because of failure to consider other factors in evaluating the results.

Chapin, Laurence D.: The Treatment of Heart Disease in General Practice. New England J. Med. 205: 220, 1931.

The author relates briefly his opinions regarding the general aspects of various forms of heart disease as formed from general practice. His own personal experience with his family led him to a keen interest in this subject which he has followed for a great many years. The material is general in nature but is interesting to record.

Ramsay, Robert Ewart, and Crumrine, R. M.: Coronary Thrombosis, in an Infant Aged Four Months. Am. J. Dis. Child. 42: 107, 1931.

Autopsy on the body of a girl aged four months eight days revealed coronary thrombosis. A photograph of the heart shows a thrombus in the vessel cut transversely in the distal portion of the vessel distended by the thrombus in situ. The wall of the left ventricle showed dimpling due to thinning of the muscle. A detailed description of the pathologic process appears in this report. The infant had been slightly ill with symptoms suggestive of some hidden infection. Following apparent recovery she became suddenly ill with distress and difficult breathing; death occurred in a few hours.

Microscopic examination is in agreement with the summary of the gross examination and confirms the supposition that the original lesion of the coronary artery was of an infectious nature, probably bacterial embolus. The embolus grew in the artery and produced increasing thrombosis until the occlusion was complete.

Schwab, Edward H., and Sanders, C. B.: Aortic Aneurysm Rupturing Into the Conus Arteriosus of the Right Ventricle. Am. J. M. Sc. 182: 208, 1931.

A case of acquired aneurysm of the ascending aorta with rupture into the conus arteriosus of the right ventricle is reported. The resulting physical signs simulate very closely those of congenital heart disease.

Reid, William D.: Congenital Dextrocardia; An Apparently Unique Case. New England J. Med. 205: 151, 1931.

A case is reported of congenital dextrocardia of the nonmirror image type and acquired stenosis of the aortic valve. A full report, including the findings on postmortem examination is included. It is interesting that the roentgen plate confirmed the clinical diagnosis of dextrocardia and by means of the fluoroscope it was disclosed that the cardiac apex was located in its normal relationship to the remainder of the heart, rather than to the right as in the mirror image type of dextrocardia. The case appears to be unusual also in that this type of congenital dextrocardia occurred without other congenital malformations of the heart.

Arnett, John H., and Long, Charles-Francis: A Case of Congenital Stenosis of the Pulmonary Valve With Late Onset of Cyanosis. Am. J. M. Sc. 182: 212, 1931.

A case of a patient with simple congenital pulmonary stenosis is presented, who after an exceeding athletic career gradually developed localized areas of cyanosis believed to be due to the stasis of blood within dilated minute blood vessels of the skin. Physical examination established a diagnosis of heart disease suggestive of pulmonary stenosis. This was confirmed at autopsy. Death in this case came at the age of thirty-three as a result of carcinoma of the pancreas. Attention is called to the fact that cyanosis due to vascular stasis is not uncommon in congenital cardiac disease and occurs in other conditions as well.

Ayman, David: Essential Hypertension. The Diastolic Blood Pressure: Its Variability. Arch. Int. Med. **48**: 89, 1931.

In seventy-six unselected, untreated patients with essential hypertension, the diastolic blood pressure was found to fluctuate widely during periods of observation extending in the individual case up to one and one-half years. The series of patients included those with advanced essential hypertension as well as those with milder forms. It was found that in all cases the diastolic blood pressure fluctuated over a wide range. The percentage of fluctuation was found to be as great as that of the systolic blood pressure. There was no appreciable difference between patients with severe hypertension and those with milder forms.

The degree of fluctuation was found to vary to a certain extent with the number of observations made on the patient: the more frequent the observations, the greater the fluctuation recorded. The lowering effect on the diastolic blood pressure of sitting in a quiet room also seems definite and conversely, the elevating effect of excitement. There were no patients who had a fixed nonfluctuating hypertension.

Sanders, Audley O.: Postural Hypotension. Am. J. M. Sc. **182**: 217, 1931.

In this case the symptoms of anemia of the brain came regularly with the upright position and promptly disappeared with the lowering of the head to body level. These phenomena recurred quite constantly over a period of years. It is of special interest in this case that the symptoms began on a definite date with a definite experience. It seemed reasonable to assume that a lesion of the autonomic system was incurred at that particular time.

McIlroy, Dame Louise, and Rendel, Olive: The Problem of the Damaged Heart in Obstetrical Practice. J. Obst. & Gynec. Brit. Emp. **38**: 7, 1931.

The present communication is based on a series of 200 cases of heart disease in 226 pregnancies which have been investigated during the last six years. The numbers occurring in the different classes were as follows:

	PRIMIGRAVIDAE	MULTIPARAE	TOTAL
Class I	35	23	58
Class II (a)	48	47	95
Class II (b)	14	49	63
Class III	2	8	10
	99	127	226

The enormous relative increase of multiparae in Group II (b) emphasizes the fact that multiple pregnancies tend to lower the cardiac efficiency permanently. The actual anatomical lesion found appears to have very little bearing on the prognosis except in so far as the severer lesions obviously produce a greater mechanical strain.

The efficient treatment of heart disease complicated by pregnancy depends upon early antenatal examination and the cooperation between the obstetrician and the cardiologist. The establishment of antenatal cardiac clinic is an essential part of an obstetrical hospital.

Skilled medical treatment has diminished to a considerable extent indication for the artificial termination of pregnancy. Heart disease of moderate severity does not preclude successful pregnancy provided that efficient care throughout antenatal period, delivery and post natal period is exercised. The chief factor is rest. One must, however, bear in mind that every pregnancy is a big strain on the damaged heart and that even in the milder cases, recovery of its former functional efficiency will take time and in spite of every attention may be incomplete. In

severer cases, there is a distinct possibility of transferring a patient into a heart category of lower grade.

It is more important to prevent a pregnancy taking place than to terminate it, since termination is only likely to be successful if performed in the early stages of pregnancy.

Rest, diet and general hygiene are of greater importance than drugs in the successful management of heart disease complicated by pregnancy. Labor should be made as easy as possible by the employment of sedatives and intermittent anesthesia. Delivery by forceps may be indicated in order to shorten the second stage in severe cases.

Yater, Wallace M., and Trewhella, Arthur P.: The Case For and Against the Operative Treatment of Angina Pectoris. Am. J. M. Sc. 182: 35, 1931.

The authors report a case of angina pectoris which had been severe enough to warrant the use of surgical procedure. They have also studied from the literature a group of 138 cases on whom neurectomy had been done for angina pectoris. They believe that the operative treatment for angina pectoris at present should be performed only in selected cases and by neurosurgeons who wish to study carefully the anatomy and physiology of the innovation of the heart and aorta and the reasons for the postoperative complications.

Levy, Robert L., and Moore, Richmond L.: Paravertebral Injections of Alcohol for the Relief of Cardiac Pain. Arch. Int. Med. 48: 146, 1931.

The authors have reviewed the literature, reporting fifty-seven cases and have described their observations on nine patients treated by them with paravertebral injections of alcohol for relief of cardiac pain. The technic of injection as described is relatively simple but the authors believe it requires skill acquired by experiments on a cadaver.

They believe that there is relief of pain in a large number of patients and in one case, there was complete relief for sixteen months. There were no unfortunate results following the injection; occasional discomfort, fever, etc., may be noted. Two patients had effusion into the left pleural cavity following the injections.

Paravertebral injection of alcohol offers a reasonably good hope of some relief to patients with paroxysmal cardiac pain. Final judgment as to its value and limitations must be reserved until more cases have been observed over longer periods of time. For the present, it should be tried only after carefully planned medical treatment has failed to alleviate intense suffering. The method has a sound physiologic basis and is less dangerous than cervical sympathectomy. The basic pathologic condition in these patients is entirely unaltered, therefore patients in whom pain has served as a danger signal of overexertion should be warned, if relieved from attacks, against exceeding the functional capacity of the heart.

Book Reviews

HEART DISEASE. By Paul Dudley White. The Macmillan Company, New York, 1931. Pp. 931, 119 illustrations.

The author states that the need for a clear, concise and comprehensive presentation of the diagnosis and treatment of heart disease in the light of our present knowledge caused him to write this book. It is intended chiefly for the use of students and practitioners. The book has been divided into four parts: the first deals with the examination of the patient and the analysis of his symptoms and signs; the second discusses the etiological types and causes of heart disease; the third deals with the structural changes present in the heart and great vessels; the fourth takes up disorders of function.

Not so many years ago the heart might justly have been considered a narrow field for specialization. Newer methods and rapid extension of knowledge have already made it difficult to keep fully abreast solely with the clinical aspects of the subject. Consequently in a book of this type in which there is great need for selection of material and condensation demanding the exercise of knowledge and judgment, one expects to find high lights and shadows. To the credit of the author be it said that the high lights are many, the shadows few and rarely dense. The book shows clearly the results of careful effort in its preparation. It has been shorn of most of the traditional error and deadwood that usually cling to textbooks.

The most valuable discussion in the book is that which deals with the patient's history. The art of history taking in these days of standardized forms is in danger, unless there are to be found those who will resolutely oppose the tendency to regard tabulation of symptoms, valuable though these may be for statistical purposes, as a satisfactory history. The author has not permitted himself to be misled by the glamour of newer methods of study into minimizing the value of the history. On the contrary he recognizes the fact that the more one knows of heart disease, the better the history he should be able to obtain.

In the section on physical examination, the part entitled "Examination other than Cardiac" might have been further elaborated with profit. The least satisfactory presentation in the book is that dealing with auscultation. This is perhaps not the fault of the author; advance in this field seems to have stopped with Potain. Unfortunately there have been reproduced many of the sound tracings published by Lewis apparently without realization, at least without mention, of the

limitations of these tracings. There are numerous positive statements in this section which the reviewer believes to be either actually erroneous or subject to qualification.

The text of the chapter on the highly important subject of cardiovascular roentgenology is not quite up to the general standard of the book, although the illustrations are excellent. The author regards the cardio-thoracic ratio as the most useful single calculation of heart size. He barely mentions the area of the antero-posterior silhouette although this calculation is probably far more significant than that of the cardio-thoracic ratio. The importance of oblique views is appreciated but, curiously, nothing is said of the lateral view.

The discussion of etiological factors is in some respects inadequate. This applies particularly to infections other than rheumatic fever and syphilis, and to a chapter designated "Other Etiological Factors and Relationships." The extreme importance of etiology warrants more complete presentation, even at the expense (if necessary) of other subjects.

The chapters on electrocardiography, abnormalities of cardiac mechanism, angina pectoris, neurocirculatory asthenia are particularly well done. The discussion of treatment seems remarkably sound. The author has apparently divested himself completely of therapeutic superstition.

A pleasing feature is the inclusion of extracts from papers of historical importance, thus adding greatly to the interest of the book and providing the reader with some of the background necessary to appreciate the present status of knowledge. It is to be hoped that these skillfully selected extracts will help to stimulate more widespread interest in the medical classics.

The bibliography is excellent. The author wisely refrains from cluttering the text with references. At the end of the book titles are arranged according to subject. Thus the reader has assembled for him a set of references which covers satisfactorily practically all subjects falling within the scope of the book.

The book should serve admirably either as a text or reference work for practitioners. It will repay careful study by all who are interested in diseases of the heart. It is too long for routine use by undergraduates, curricula being as they are, but it may be warmly recommended to students who are attracted to the study of heart disease.

C. C. W.

THE FACTOR OF INFECTION IN THE RHEUMATIC STATE. By Alvin F. Coburn. Williams and Wilkins Company, Baltimore. Pp. 288, fully illustrated, with 7 color plates.

This book is the published results of a study of the rheumatic state in its many phases. The work has been done principally at the Pres-

byterian Hospital in New York and with a small colony of rheumatic subjects in Porto Rico. The study has been essentially clinical in nature, dealing principally with the field of bacteriology and the observation of patients with rheumatic fever. The reviewer finds himself so fully in accord with the ideas expressed in the text and with the observations made on patients that it is difficult to do anything less than recommend the book in most enthusiastic terms.

The scope of the book deals with the impressions that exist at present concerning the rheumatic state. This term is used by the author to include that great mosaic of disease manifestations which in the past has been described under the title of "acute articular rheumatism" and which is now usually entitled "acute rheumatic fever." Except for bacteriological studies of the body tissues and blood, certain anatomical changes of material removed at necropsy and a few serological tests, the book is devoted almost exclusively to the description of clinical manifestations of this disease.

The outstanding feature of the text is the very large amount of clinical material presented in the form of brief case reports illustrating the many ideas expressed by the author. These case reports are interesting and show clearly what occurs in many patients. The case reports are inserted directly in the text. The scope of the book is necessarily limited to this field because, as the author states, this disease does not readily yield itself to any other means of investigation. While it is strongly suspected and probably accepted that the streptococcus is the etiological agent, yet it is difficult to recover the organism from the host, and as yet no suitable animal has been found which yields itself to experimentation. This feature of the rheumatic state, as is well known, makes it difficult to subject this disease to satisfactory scientific laboratory investigation. However, the author's method of handling the subject is a very good example of proper clinical scientific investigation.

It would be difficult to take up all the ideas expressed by the author for analysis. There are many important ones and only a few can be mentioned.

Chapter I deals with the rheumatic state. This description is clear and presents a very comprehensive idea of this protean disease, as it is understood at the present time.

Chapter II is devoted to the author's bacteriological studies on two important phases of the disease: (1) the incidence of a bacteremia; (2) an investigation of bacterial endocarditis and its association with the rheumatic state. In this study a bacteremia was only occasionally found in patients with the disease. In patients with high fever and other symptoms which suggested such a bacteremia it was possible to recover organisms occasionally, usually streptococci, from the circulating blood with careful cultural methods. However, a very large

number of patients showed sterile cultures. It is believed that bacterial endocarditis is a form of heart disease associated with some other injury in the heart and that while bacterial endocarditis may be superimposed on rheumatic carditis or may exist in the same patient at the same time, the two conditions are separate and distinct. These ideas are in accord with those generally held by other workers.

Chapters III and IV deal with some general impressions and observations of rheumatic disease as it appears on the Presbyterian Hospital Wards in New York. These observations are related to the annual and seasonal variations of the disease, its regional distribution, the question of the "rheumatic family" and other equally important features of the disease. It is important to note that the author found rheumatic manifestations among immigrants newly arrived from regions which are ordinarily free from rheumatic infection. It was observed that a group of rheumatic individuals taken from New York City to Porto Rico became relatively free of the disease after several weeks' residence in the tropical region and that their disease reappeared when they returned to New York.

Chapter V deals with observations on the upper respiratory bacterial flora in man and its relationship to the rheumatic state. This includes a study of the tonsils removed at operation as well as the cultural studies of the flora of the upper respiratory area. In Chapter VII the question of tonsillectomy in individuals with rheumatic fever is discussed. It is pointed out that recrudescence of the disease frequently follows such an operation. In this same chapter the relationship between scarlet fever and rheumatic fever is also discussed. The author believes that scarlet fever is related to the rheumatic process in some individuals who gave no clinical evidence of being stigmatized with the rheumatic state, and found that it appeared to be responsible for several recrudescences of the disease in others. All the facts collected during this study point to the importance of scarlet fever as a factor of infection in the rheumatic state.

Chapter VI deals with reactions of the skin to intracutaneous injection of bacterial nucleoproteins.

It is not the scope of this book to present the historical side of rheumatic fever; as stated above, it is principally concerned with the author's observations of the condition as it exists at the present time.

The bibliography includes all the important writings on the various phases of this subject and is exceptionally well selected.

The form of the book is excellent. It is well printed, the illustrations, including a frontispiece showing a composite picture of the disease, are unusually good and there are numerous helpful charts.

H. McC.

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